Abstracts

NASPGHAN ANNUAL MEETING
OCTOBER 18 – 20, 2012
SALT LAKE CITY, UT

ABSTRACTS

(*Poster of Distinction)

POSTER SESSION I
Thursday, October 18, 2012

Esophagus/Stomach

1 HISTOLOGICAL RESPONSE TO PROTON-PUMP INHIBITOR THERAPY OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN. Amir Abdel-Wahab1, Sarangarajan Ranganathan1, Margaretha Casselbrant1, Alka Goyal2. 1Pediatrics, University of Pittsburgh, Pittsburgh, PA; 2ENT, University of Pittsburgh, Pittsburgh, PA

Background: Eosinophilic esophagitis (EoE) patients frequently have symptoms overlapping with gastroesophageal reflux disease (GERD). While the current practice guidelines have created a category of PPI responsive EoE, results of PPI therapy have not been systematically evaluated.

Aims: To study the histological responses on esophageal biopsies in pediatric patients with EoE. To analyze clinical symptoms before and after PPI therapy.

Methods: A retrospective chart review was performed on 41 consecutive patients with EoE who had undergone esophageal biopsies before and after PPI therapy; patients treated with steroids were excluded. Esophageal eosinophilia (>20 per high-power-field, HPF) was required for a diagnosis of EoE and histological response was defined as reduction in eosinophil count to <10 per HPF or return to normal histologically.

Results: Mean age at diagnosis was 7.3 y (range: 1-21 y); 29 male and 12 females. Symptoms prompting evaluations were vomiting/regurgitation (68%), history of allergies (66%), abdominal pain (56%), cough (29%), dysphagia (27%), recurrent otitis (22%), recurrent otitis (22%), sleep apnea (17%), hoarseness (17%), asthma (15%) and sinusitis (4%). Eight out of 41 patients (19.5%) showed histological response. Seventeen out of 41 patients (41.4%) improved clinically; 12/17 (70%) of these patients did not show a histological response. No particular symptom including history of allergy or asthma was predictive of PPI response.

Conclusion: In this study, one in five patients diagnosed with EoE showed histological response to PPI. There was no clear relationship between symptoms and histological responses and follow-up biopsies may be indicated to help guide further therapy.

2* OUTCOMES AND MANAGEMENT OF PEDIATRIC COLLAGENOUS GASTRITIS - METANALYSIS OF POOLED NEW AND PUBLISHED CASES. Thomas M. Attard, Nadia M. Hijaz, Seth S. Septer. Pediatric Gastroenterology, Children's Mercy Hospital, Kansas City, MO

Background: Collagenous gastritis (CG) is characterized by patchy subepithelial collagen bands. The natural history and best management in children are unknown. Herein we present a pooled analysis of our observations on two patients with the peer reviewed publications on the outcome and treatment options.

Methods: We performed a search in Pubmed, Medline and Embase for related terms; articles including management and clinical and/or endo-histologic follow up information were included. Reported findings were pooled in a dedicated database including corresponding data extracted from chart review in our patients with CG.

Results: There were 19 patients (13F) with a mean age (SD) 11.0 (4.7) years. The clinical presentation included iron deficiency anemia with dyspeptic symptoms. The reported duration of follow up (in 15 patients) ranged (mean) between 0.2 - 14 (3.9) years. The treatment modalities included oral iron (11), antisecretory measures (12); PPI (9), H2RA (2) other (1), sucralfate (4), prednisolone (4), oral budesonide (3/1 in fish oil) and triple therapy (3) (H. pylori pos.). Misoprostol, furazolidone, metronidazole, exclusion diet and parenteral nutrition were added in isolated cases. One patient showed no clinical improvement; all others improved ranging from complete symptom resolution (7/17), improved dyspepsia (10/17) with intermittent symptoms (4).

Follow up endo-histopathologic data (10 patients) included persistent collagen band; unchanged (8) and decreased/resolved (1). MN infiltrate; increased, stable and decreased in 3, 4 and 2 patients respectively. Neither correlated with clinical course. Intestinal metaplasia and endocrine cell hyperplasia were reported (1) raising the concern of long term malignant transformation.

Conclusions: Pediatric CG generally entails a favorable prognosis, most patients require iron supplementation and are treated with antisecretory medicines albeit response rate is unknown. There appears to be poor correlation between treatment modalities, clinical improvement and endoscopic-histologic abnormalities.
3  MULTICHANNEL INTRALUMINAL IMPEDANCE (MII) USED TO EVALUATE ASSOCIATED GASTROESOPHAGEAL REFLUX (GER) WITH APPARENT LIFE THREATENING EVENT (ALTE), APNEA AND DESATURATIONS IN INFANTS AND TODDLERS. Karla J. Au Yeung, Eric Tibesar
Pediatrics, Johns Hopkins Hospital, Baltimore, MD
Introduction: Proving association between GER and respiratory events such as ALTE, apnea, or desaturations in infants and toddlers, has been a problem for clinicians. Multichannel intraluminal impedance (MII) is used to measure GER and assess association with abnormal respiratory events. Furthermore, due to comorbidities seen in infants and toddlers with respiratory difficulties, patients may be fed via nasogastric or gastrostomy tubes; however, there are no known normal values for MII measurement for tube fed patients, which confounds interpretation of results. Methods: We retrospectively reviewed charts from 29 infants and toddlers who underwent a 24 hour study with MII measurement to evaluate GER and its association with respiratory abnormalities. The MII was ordered as clinical evaluation for inpatients and outpatients to rule out GER. Results: Average age was 5.7 months, range 10 days to 2.7 yrs old (only 2 patients > 1yo). Comorbid conditions included prematurity, congenital heart disease, genetic syndrome, congenital airway anomalies, and pulmonary hypertension. Positive symptom index (SI) was seen in 11/29 (38%), positive symptom association probability (SAP) occurred in 10/29 (34.5%), and for both was 8/29 (27.6%). Comparing tube fed (16) versus non-tube fed (13) groups, frequency of reflux based on impedance was similar (63.2 ± 30.3 versus 56.6 ± 54.3, p = 0.70). The impedance values for the group who was referred for G-tube/Nissen was 65.6 ± 66.7 versus without a referral was 53.4 ± 28.3, p = 0.84. Referral for G-tube alone was also not significant. Conclusions: Approximately 1/3 of reflux events showed association with ALTE, apnea, or desaturations in infants and toddlers in infants demonstrating clinically significant respiratory difficulties. MII results had no impact on the decision towards surgery. Performing MII studies in children with tube feeding seems to give reliable results.

4  RELATIONSHIP BETWEEN BODY MASS INDEX AND GASTROESOPHAGEAL REFLUX IN CHILDREN EVALUATED WITH 24-HOUR MULTICHANNEL INTRALUMINAL IMPEDANCE-PH MONITORING. Eric Chiou, Bruno Chumpitazi, Pediatrics, Baylor College of Medicine, Houston, TX
Background: Obesity has been associated with gastroesophageal reflux disease (GERD), but the pathogenic mechanisms responsible for this relationship are still unclear.
Aim: To evaluate the association between body mass index (BMI) and GERD in children as detected by multichannel intraluminal impedance-pH (MII-pH) monitoring.
Methods: Retrospective review of 82 consecutive MII-pH studies of pediatric patients, aged 2-18 years. Patients were divided into normal (BMI percentile <85) and overweight/obese (BMI percentile ≥ 85). Gastroesophageal reflux (GER) episodes were classified as acid reflux (AR), nonacid reflux (NAR), and total number of GER episodes, as detected by MII-pH. We also assessed the number of reflux episodes while supine and the number episodes with proximal extent. We evaluated the symptoms associated with reflux by using the symptom index (SI) and symptom association probability (SAP).
Results: The total number of GER episodes and NAR episodes were significantly increased in patients with elevated BMI (see Table). There was no significant difference between groups in AR or percent time with pH<4. Patients with elevated BMI also had significantly higher amounts of reflux while supine. There was no significant difference in symptom correlation between groups.
Conclusions: Elevated body mass index in children is associated with increases in total, nonacid and supine GER episodes. Further studies will need to investigate the role of factors such as intragastric pressure in overweight and obese children with GERD.

| Association between body mass index (BMI) and different reflux parameters |
|-----------------|-------------------|-----------------|
|                   | Normal BMI (n=61) | Overweight/Obese BMI (n=21) | p value |
| Percent time pH<4 | 2.3 (0.6-5.4)     | 2.9 (0.6-7.7)     | 0.569   |
| Total GER Episodes | 35 (17-58)        | 61 (33-86)        | 0.018   |
| AR Episodes       | 11 (2.5-28.5)     | 21 (6.5-36.5)     | 0.209   |
| NAR Episodes      | 16 (8-29)         | 25 (15-52)        | 0.03    |
| Supine GER Episodes | 5 (2-9.5)        | 11 (4.75-21.75)   | 0.01    |
| Proximal GER Episodes | 6 (2-14)        | 12 (4.5-21.5)     | 0.108   |

Results are expressed as median (25-75th percentile)
5  CAN IMPEDANCE BASELINE REFLECT ESOPHAGEAL INTEGRITY? Judith Cohen Sabban¹, Gabriela Donato¹, Silvia Christensen¹, Teresa Davila², Marina Orsi¹, ¹Hospital Italiano, Buenos Aires, Argentina; ²Hospital Garrahan, Buenos Aires, Argentina

It has been suggested in animal models and adults that the Multichannel Intraluminal Impedance (MII) baseline reflects the integrity of the esophageal mucosa, being lower in patients with esophagitis than in those with normal mucosa.

Aim: To compare the impedance baseline values in patients with and without esophagitis.

Material & Methods: Review of MII tracings performed between May 2008 and June 2012, in children suspected of having gastroesophageal reflux. All patients underwent upper endoscopy with multiple esophageal biopsies followed by a 24 hr MII-pH study. Esophageal histology was reported by two independent pathologists in a blinded manner. MII tracings were analyzed manually by two physicians using Sandhill software. Mean IB was measured retrospectively by 6 channel impedance testing at every hour for 24 h impedance-pH recording, excluding swallows and reflux. Student’s T-test was used for statistical analysis. Patients with eosinophilic esophagitis were excluded.

Results: Tracings of 60 children were evaluated; mean age: 9.78 yrs (r3-17yrs) 45 of which could be properly analyzed: 26 with esophagitis (E) and 19 with normal mucosa (N). E: 20/26 had mild esophagitis (Ea) and 6/26 had moderate to severe esophagitis (Eb). Significant differences were observed when Eb was compared with N, but not with Ea.

Conclusions: The evaluation of the IB may be a valuable method to predict esophageal mucosal integrity. Although it is time consuming it may be of particular help in infants and to select patients for endoscopy in cases of potentially high risk patients.

Results

<table>
<thead>
<tr>
<th>Moderate to severe Esophagitis (Omhs) Eb (X±SD)</th>
<th>Normal mucosa(Omhs) (X±SD)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel 1 2977.5 ± 412.62</td>
<td>2500 ± 670</td>
<td>t-1.63</td>
<td>0.116</td>
</tr>
<tr>
<td>Channel 2 1878 ± 346.67</td>
<td>2136.8 ± 714.69</td>
<td>t 0.845</td>
<td>0.4</td>
</tr>
<tr>
<td>Channel 3 2088 ± 615.39</td>
<td>2222.4 ± 590.12</td>
<td>t 0.48</td>
<td>0.635</td>
</tr>
<tr>
<td>Channel 4 1916.5 ± 617.55</td>
<td>2782.9 ± 740.69</td>
<td>t 2.58</td>
<td>0.01</td>
</tr>
<tr>
<td>Channel 5 926.17 ± 316.58</td>
<td>2068.9 ± 537.3</td>
<td>t 4.9</td>
<td>0.000</td>
</tr>
<tr>
<td>Channel 6 860 ± 343.54</td>
<td>2080.9 ± 874.96</td>
<td>t 3.3</td>
<td>0.003</td>
</tr>
</tbody>
</table>

6  COMPARATIVE EFFECTIVENESS OF PROTON PUMP INHIBITOR VERSUS H2-RECEPTOR ANTAGONIST THERAPY FOR GASTROESOPHAGEAL REFLUX DISEASE. Robert Davis, Rebecca Scherr, David A. Gremse, Pediatrics, University of Nevada School of Medicine, Las Vegas, NV

Background: Proton pump inhibitors (PPIs) are reported to be more effective than H2-receptor antagonists (H2RAs) for the treatment of gastroesophageal reflux disease (GERD) in adults. The aim of this study was to assess the comparative effectiveness of PPI versus H2RA therapy for the treatment of GERD in infants.

Methods: Records of infants 1 to 12 mo. of age with GERD were reviewed. Treatment outcome was assessed by the GERD Assessment Symptom Questionnaire (GASQ) (JPGN 2005;41:178-185). Baseline GERD symptoms at visit 1 were assessed after 1-month of H2RA therapy. Ranitidine was stopped and a PPI was prescribed. GERD symptoms were re-assessed after 4 weeks of PPI therapy. The difference in GASQ scores from H2RA and PPI therapy in the treatment group was compared to a control group of 16 infants who were treated with ranitidine over a similar length of time. Outcomes were compared using paired t-test. Results: 57 infants (25 males, age 3.1 ± 2.0 mo., mean ± SD, 69% Caucasian, 26% Hispanic, 5% African-American) with GERD diagnosed by GASQ scoring were studied. Dietary history showed: breast milk (37%), protein hydrolysate formula (26%), cow milk formula (18%), commercially thickened formula (12%), and amino acid-based formula (7%). There were no significant differences in the rates of breastfeeding or the type of formula feedings in the PPI treatment or H2RA control groups. The GASQ scores after 4 weeks of ranitidine therapy at visit 1 were compared to GASQ scores after 4 weeks of PPI therapy on visit 2. The GASQ score results are shown in the table.

Conclusions: The results showed that GERD symptoms in patients 1 month to 1 year of age significantly decreased after PPI therapy compared to the GERD symptoms observed during treatment with ranitidine. We conclude that acid suppression therapy with PPIs yields a greater reduction in GERD symptoms than ranitidine therapy in infants.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>GASQ Score-Visit 1 (H2RA)</th>
<th>GASQ Score-Visit 2 (H2RA or PPI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2RA vs. PPI (n=41)</td>
<td>287.1 ± 204.1</td>
<td>90.1 ± 86.7</td>
<td>0.0000002</td>
</tr>
<tr>
<td>H2RA vs. H2RA (n=16)</td>
<td>114.8 ± 90.8</td>
<td>95.4 ± 111.5</td>
<td>0.50</td>
</tr>
</tbody>
</table>
7 HYPOMAGNESEMIA IS NOT ASSOCIATED WITH CHRONIC PROTON PUMP INHIBITOR (PPI) USE IN PEDIATRIC PATIENTS. Joan S. Di Palma, Suzanne C. Kenyon, Sheeba K. Abraham, Fernando del Rosario, Gastroenterology, Nemours Children's Clinic, Philadelphia, PA

Objective: Hypomagnesemia has been reported in adults, resulting in a variety of symptoms. In March 2011, the FDA recommended obtaining magnesium levels in patients on prolonged PPI therapy. Magnesium levels in children on chronic PPI therapy have not been evaluated. Therefore we have initiated an ongoing evaluation of magnesium levels in pediatric patients on chronic PPI therapy.

Methods: We obtained magnesium levels on 53 children (30F, 23M), age range 1.75 - 20yrs (mean=10.2yrs) from January 2011 - May 2012. Length on PPI therapy at least 4-106 mos (mean=29.3mos)

Patients were on one of the following PPI's with doses measured in mg/day: lansoprazole 15-30 (n=26), omeprazole 10-40 (n=16), esomeprazole 20-40 (n=6), pantoprazole 40-60 (n=2), dexlansoprazole 30-60 (n=2), omeprazole and sodium bicarbonate 40 (n=1)

Patients' diagnosis were gastroesophageal reflux (n=45), inflammatory bowel disease (n=3), dysphagia (n=1), esophageal atresia (n=1) gastritis (n=2). No patient had renal or cardiac disease.

Results: No patient had an abnormal magnesium level. Magnesium levels ranged from 1.8-2.4mg/dl (mean=2.155mg/dl)

Conclusion: Hypomagnesemia was not demonstrated in pediatric patients >1yr of age on chronic PPI therapy. Magnesium levels in infants <1yr of age and in children on chronic PPI therapy with co-morbidities such as cardiac and renal disease were not studied. It would be of benefit to include this group in further studies.

8 THE NEWBORN LAMB AS A NEW MODEL FOR STUDYING GASTROESOPHAGEAL REFUX. Djamal-Dine Djeddi, Nathalie Samson, Jean-Paul Praud, Department of Physiology and Pediatrics, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada

Introduction: To our knowledge, there is no animal model of neonatal gastroesophageal reflux (GER). Meanwhile, ovine models have been used for studying numerous physiological processes and pathological conditions in the neonatal period for over a century.

Objective: We aimed to determine whether the newborn lamb at term is a valid model for studying GER.

Subjects and methods: Seven bottle-fed lambs, aged 2-3 days, underwent esophageal Multichannel Intraluminal Impedance-pH monitoring (MII-pH).

Results: A total of 196 reflux episodes were recorded, including 73% alkaline and 27% weakly acid. No acid refluxes were observed. Median bolus clearance time was 4s [3 ; 5.5], and mean proximal reflux extent was 35% (26).

Conclusions: This first report of MII-pH in the newborn mammal sets the foundations for future studies with physiological and clinical relevance to human neonates such as apneas-bradycardias, hypoxia, nasal respiratory support, as well as for assessing the effects of future medications against GER.

9 TUMOR SUPPRESSIVE GENE P-53 AND CELL PROLIFERATION MARKER KI-67 IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS. Yoram Elitsur1, Awni Al-Subu1, Krista L. Denning2, 1Pediatrics, Marshall University, Huntington, WV; 2Pathology, Marshall University, Huntington, WV

Background: Eosinophilic esophagitis (EoE) has been recognized as a chronic disease of the esophagus in children and adults. Chronic inflammation of the esophagus may lead to malignant transformation of the cells. P-53 is a mutated intracellular oncogene marker, and Ki-67 is a nuclear antigen associated with cell proliferation. Both markers were increased in patients with Barrett's esophagus and esophageal cancer. Aim: To assess P-53 and Ki-67 in children with EoE before and after therapy. Methods: Esophageal biopsies from children with EoE (test), GERD (Control 1), and normal esophagus (Control 2), consisted our patient population. Ten EoE children with successful treatment participate in the 2nd part of the study. The monoclonal oncogene P-53 (DAKO, DO-7) and Ki-67 cell marker (DAKO, Clone MIB-1) were utilized. Immunoreactivity of P-53 and Ki-67 was defined positive when at least 10% of the cells stained positive (Wang 1993). Ki-67 immunoreactivity was calculated as a percentage of positive cells per 500 cells (Feith 2004). Biopsies from 3 adult pts with esophageal cancer were also used as control. Immunoreactivity was compared among the groups and between children with EoE before and after therapy.

Results: Immunoreactivity of P53 and Ki-67 in children with EoE was significantly higher than in Control groups, not to GERD group (Table 1). A significant reduction in eosinophils (41 vs. 5.6/HPF, p=0.0003), P-53 (70% vs. 0%, p=0.003), and Ki-67 (59% vs. 23%, p=0.003) was noted in EoE group post therapy. Conclusion: Oncogene P-53 and Ki-67 immunoreactivity were higher in the EoE compared to the normal group. The decrease in immunoreactivity for P-53 and Ki-67 after treatment may represent cell proliferation phenomenon rather than early markers for cancer development (dysplasia).

EoE and cell markers
10 SIMULATION AND PERMUTATION METHODS FOR THE DETERMINATION OF TEMPORAL ASSOCIATION BETWEEN APNEA AND REFLUX. THE SYMPTOM INDEX P-VALUE AND SYMPTOM SENSITIVITY INDEX P-VALUE. Daniel R. Glen1, Peter Murakami2, Jeanne Nunez3, 1Scientific and Statistical Computing Core of the NIMH Intramural Research Program, NIMH, NIH, Bethesda, MD; 2The Johns Hopkins Biostatistics Center, The Johns Hopkins University, Baltimore, MD; 3Pediatrics, Division of Neonatology, The Johns Hopkins Medical Institutions, Baltimore, MD

Background: The SAP (symptom association probability), the current method to determine temporal association (TA) between reflux and symptoms, has limitations due to the constraints of binning and the violation of statistical principles of the Fisher exact test that lead to an invalid estimation of TA.

Objective: To develop methods of simulation and permutation to compute the TA between apneic and reflux events and to compare these to the SAP.

Design/Methods: TA was analyzed between polysomnographic obstructive apneas and Multi-channel Intraluminal Impedance (MII) reflux in four former premature infants with persistent apneas at term. The experimentally found association was compared to the association observed in simulated or permuted data consistent with the lack of association beyond what is expected by chance alone. TA was computed based on symptom and symptom sensitivity indices, SI and SSI, with varying window of association (WA) times from 15 to 300s.

Results: The three methods estimated p-values at varying WA that generally followed the same pattern of the SAP which had a more erratic pattern. The process of binning may explain the erratic pattern of the SAP leading to an over and underestimation of the p-values.

Conclusions: Each of the new methods produced p-value results consistent with each other and the SAP, yet were not subject to its limitations. These methods are called SIP and SSIP, Symptom Index and Symptom Sensitivity Index p-values. The new application of simulation and permutation methods to estimate a TA may be used not only for the TA between apnea and reflux but also between any symptoms and reflux or any categorical events.

11* RANDOMIZED, BLINDED, PLACEBO-CONTROLLED 1 YR STUDY OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) THERAPY IN THE MANAGEMENT OF CHILDHOOD ASTHMA. Benjamin D. Gold1, Bonney Reed-Knight1, Randall Brown2, Jeffery Lewis1, Burton Lesnick2, 1Children's Center for Digestive Healthcare, Atlanta, GA; 2Georgia Pediatric Pulmonology Associates, Atlanta, GA

Intro/Objective: NIH-funded RCTs of GERD treatment in adult and childhood asthmatics demonstrated no difference between placebo and acid suppression in asthma outcomes; other uncontrolled studies showed asthma improvement. We enrolled moderate to severe asthmatics (4-11 yrs old) into a study of 1 yr duration to determine if GERD treatment improved asthma outcomes.

Methods: After informed consent, pts were randomized to lansoprazole (1.5 mg/kg/dose bid; max 60 mg/day) or placebo. Asthma exacerbations, asthma control (ACQ) and quality of life (AQOL) and GERD symptoms were characterized @ 6 wk intervals x 1yr; baseline allergy testing also performed.

Results: 58 children were prospectively randomized; 26 assigned to receive lansoprazole, and 32 to receive placebo. Independent samples tests, χ2 tests revealed no significant differences between the two treatment groups (p < 0.05) on demographic or asthma characteristics at baseline. Group differences were explored using generalized estimating equations. At the 52-week assessment point, asthma exacerbations were no different between both groups; ACQ score decreased by less than the meaningful clinically important margin in both groups (p = .99). Similarly, there were no significant treatment effects on patient-report of GERD symptoms or physician global assessment (PGSA). Analyses of the measures of lung function revealed no significant treatment effects on pre- or post-bronchodilator FEV or FVC over study duration. Although no group differences were found, a main effect of time was found for patient report of GERD symptoms, the PGSA and AQOL. Over the study duration, both treatment groups demonstrated a decrease in self-reported GERD symptoms, χ2 (1) = 30.54, p <.001, as well as an increase in quality of life, χ2 (1) = 53.58, p <.001. Conclusion: We demonstrated no difference between placebo and high dose acid suppression in asthma outcomes over a 1 yr duration. Our study, the longest RCT to evaluate acid suppression in poorly controlled childhood asthmatics, raises important questions regarding a GERD-asthma causal relationship. Support by Takeda Pharmaceuticals.
12 GASTROESOPHAGEAL REFLUX IN PEDIATRIC PATIENTS WITH CHRONIC COUGH AND CROUP. M. Greifer1, M. Santiago2, L. Smith3, J. Levine1, GI, Cohen Children's Medical Center, New Hyde Park, NY; Pulmonology, Cohen Children's Medical Center, New Hyde Park, NY; ENT, Cohen Children's Medical Center, New Hyde Park, NY

Pediatric patients with chronic cough and croup present a diagnostic and treatment dilemma. Differential diagnosis includes pulmonary, otolaryngeal and gastrointestinal causes. Our institution has created a team of physicians, the CARE (Comprehensive Airway, Respiratory and Esophageal) team to address these patients. We hypothesized that despite detailed history and exam, patients with chronic cough and croup require multidisciplinary evaluation to uncover gastroesophageal reflux.

Methods: Retrospective chart review of patients with chief complaint of chronic cough or croup. Symptoms included vomiting/spitting up ("GER"), abdominal pain and failure to thrive (FTT). Patients had upper endoscopy, bronchoscopy and laryngoscopy performed concurrently. Bronchoalveolar lavage (BAL) was also performed. Results were reviewed. The study was IRB approved.

Results: 40 patients were evaluated (mean age 5.76 ±3.9 years; 29 males). Airway abnormalities, including laryngeal findings, subglottic abnormalities and upper airway obstruction were noted in 21/40 children. BAL findings were found in 11/40. 15 patients had esophagitis on biopsy (group 1) while 25/40 had normal biopsies (group 2). There was no significant difference in ages between the groups (p=0.5). There was no significant difference based on the presence of "GER" (p=0.5), abdominal pain (p=1.0) and FTT (p=1.0). There was no significant difference based on location or presence of airway abnormality (p=0.7) or BAL findings (p=0.7). In group 1, 4/15 (27%) met criteria for eosinophilic esophagitis.

Conclusions: In our patients with chronic cough and croup, almost 40% of patients were found to have esophageal findings. Presenting symptoms were not predictive of esophagitis. Airway abnormalities and BAL findings were found in many of these patients as well. Because of the varied treatment strategies required for each specific finding, these patients benefit from a multidisciplinary evaluation approach.

13 RETROSPECTIVE ANALYSIS OF PEDIATRIC NEODYMIUM MAGNET INGESTIONS AND COMPLICATIONS AT A MAJOR SUBURBAN MEDICAL CENTER. Jody Hefner1, Catherine Chao2

1Pediatric Gastroenterology and Nutrition, Walter Reed National Military Medical Center, Bethesda, MD; 2Pediatric Digestive Disease Center, INOVA Fairfax Hospital for Children, Fairfax, VA

BACKGROUND: Rare earth (neodymium) magnet ingestions in children present a unique set of complications and management challenges. Several case reports have highlighted the dangers associated with multiple neodymium magnet ingestions. AIM: To determine the incidence of neodymium magnet ingestions in the pediatric population in a large suburban area and describe their complications and clinical course. METHODS: A retrospective analysis of pediatric patients at a single large suburban hospital was performed for April 2011 to May 2012. Medical record numbers with ICD-9 Codes 938 (Foreign Body GI NOS) and 9352 (Foreign body in stomach) were reviewed. Patients older than 18 were excluded. Records were reviewed for foreign body presence, type, location, intervention made, admission days (if admitted) and outcomes. RESULTS: 108 records contained diagnoses 938 or 9352. 91 met criteria. 11 cases (12%) were neodymium magnet ingestions. Median age was 6 years (range 2 to 12 years) and 7/11 were male. Median number of magnets ingested was 2 (range 1 to 23). EGD removal was attempted in 7 of the 11 patients and successful in 2 cases. Surgical intervention was required in 3. Surgical patient case ages were 2, 3, and 10 years of age, who ingested 10, 6, and 2 neodymium magnets, respectively. Five cases required hospital admission. Those admitted for surgical complications had average length of stay of 6 days while non-surgical admissions stayed on average for 2 days. Overall surgical complication rate, regardless of number ingested, was 27% (3/11). This rose to 50% with ingestions greater than 2 (2/4). Admission rates were 45% (5/11).

CONCLUSIONS: Neodymium magnet ingestions carry a unique increased risk of surgical complications and increased health care costs. Higher rates of complications are associated with increased number of magnets and younger age. Increased awareness for the public, as well as medical providers, is needed to emphasize avoidance and prompt evaluation when ingestion is suspected.

14 ESOPHAGO-GASTRODUODENOSCOPY (EGD) FINDINGS IN CHILDREN ASSESSED FOR FEEDING DIFFICULTIES. Punit Jhaveri1, Pooja B. Jhaveri2, Keith Williams1, Douglas G. Field1

1Pediatric GI, Penn State University, Hershey, PA; 2Allergy and Immunology, Penn State University, Hershey, PA

BACKGROUND: An estimated 25-40 % of infants experience feeding difficulties. Feeding difficulties in children can stem from organic etiologies. Medical conditions such as reflux, gastritis and eosinophilic esophagitis can play a significant role in feeding aversion. Our objective with this retrospective review is to identify medical etiologies for feeding issues as recognized by endoscopic evaluation. There is currently very limited data relating EGD findings in this population.

METHODS Between January 2007 and December 2011, 193 patients were endoscopically evaluated and assessed by the Penn State Hershey Children's Hospital Multi-Disciplinary Feeding Team. The age of the patients ranged from 2 months to 19 years, with a mean age of 3 years. The diagnosis of feeding difficulties was made by a pediatric gastroenterologist based on clinical history and data from the feeding clinic. The endoscopic findings were recorded and analyzed to determine their association with feeding difficulties.

RESULTS: Of the 193 patients, 110 had endoscopy findings that could be related to feeding difficulties. The most common findings were gastroesophageal reflux (GER) and esophagitis, which were found in 58% of the patients. Other findings included duodenal ulcers, gastritis, and eosinophilic esophagitis. The presence of GER and esophagitis was associated with feeding difficulties in 42% of the patients. The study concluded that endoscopic evaluation can help identify medical etiologies for feeding difficulties in children.

CONCLUSIONS: Endoscopic evaluation is a valuable tool in assessing feeding difficulties in children. It can help identify organic etiologies that may be contributing to feeding aversion. Further studies are needed to establish a clear association between endoscopic findings and feeding difficulties.
from 0-17 years. Forty patients underwent more than 1 endoscopy. There were 153 patients evaluated for this review.

RESULTS: Eighty-six (56%) of patients had no pathological findings. Sixty-seven patients had varying histopathologic diagnosis (see Table 1). No adverse events occurred during endoscopy.

CONCLUSIONS: The EGD is an essential tool in the evaluation of children who present with feeding aversions. Though 52% had no pathological findings, 48% were noted to have histological changes, of which reflux changes were the most common. The EGD appears to be a safe and informative tool in the diagnostic evaluation of children with feeding difficulties. These noted histologic findings may alter medical management and can certainly compliment concurrent behavioral interventions. Using our data, we hope to inform parents, general providers and specialists that the EGD remains a vital part of the multi-disciplinary approach to children with feeding difficulties.

<table>
<thead>
<tr>
<th>Histologic Findings</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pathologic alteration</td>
<td>52%</td>
</tr>
<tr>
<td>Changes associated with GE reflux</td>
<td>18%</td>
</tr>
<tr>
<td>Gastritis</td>
<td>14%</td>
</tr>
<tr>
<td>Eosinophils (&gt;15/high power field)</td>
<td>10%</td>
</tr>
<tr>
<td>Celiac Disease</td>
<td>6%</td>
</tr>
<tr>
<td>More than 1 Finding</td>
<td>7%</td>
</tr>
</tbody>
</table>

15 SYMPTOMS, ENDOSCOPIC APPEARANCE AND HISTOLOGIC SEVERITY IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS. Erika Kutsch1, Fernando del Rosario1, Matthew Di Guglielmo1, Zhaoping He1,2, Katryn Furuya1 1Gastroenterology and Nutrition, Alfred I. duPont Hospital for Children, Wilmington, DE; 2Research, Alfred I. duPont Hospital for Children, Wilmington, DE

Objective: The aim was to determine if there was correlation between the symptoms of eosinophilic esophagitis (EoE) at diagnosis and post-treatment and endoscopic appearance and histologic severity. Methods: A retrospective study was done with patients ages 1-18 years with a histologic diagnosis of EoE. As symptoms often vary by age, patients were stratified into 2 groups; 0-4 and 5-18 years. Symptoms, such as vomiting, abdominal pain, dysphagia, regurgitation were scored on the frequency of each symptom. The endoscopic score was based on the presence of furrowing, white plaques, concentric rings, edema and erythema. Histologic severity was graded based on the number of eosinophils. The symptoms of EoE at diagnosis and post-treatment were analyzed in terms of endoscopic appearance and histologic score. Results: 50 patients were studied; 14 in the 0-4 and 36 in the 5-18 year old (yo) age groups. Symptom scores in both groups improved from initial to follow-up endoscopy (P=0.006 in both groups). The mean eosinophil count in the 0-4 yo group improved in the mid and distal esophagus (P=0.009 and P=0.001 respectively) whereas there was only improvement in the distal esophagus for the 5-18 yo group (P=0.0075). In both groups, there was improvement in the mean endoscopic score, but only in the 5-18 yo group did it reach statistical significance (P<0.02). In the post-treatment 0-4 yo group, there was a strong correlation between reflux and the mid/distal esophageal eosinophil count (r=0.79 mid (P=0.001); r=0.56 distal (P=0.035)) and between abdominal pain and mid esophageal eosinophil count (r=0.58, P=0.029). In the 5-18 yo group, there was no correlation between symptoms and eosinophil count. Conclusion: Despite symptom improvement, our study only showed a positive correlation between abdominal pain and reflux in the 0-4 yo group and the number of eosinophils in the mid and distal esophagus.

Pancreas/Cystic Fibrosis

31 PANCREATIC AND BILIARY SECRETION ARE BOTH ALTERED IN CYSTIC FIBROSIS PIGS
Aliye Uc, Radhamma Giriypappu, Michelle Griffin, Lynda Ostedgaard, Xiaoxiao Tang, David Stoltz, Marwa Abu-El-Haija, Paula Ludwig, Alejandro Pezzulo, Maisam Abu-El-Haija, Peter Taft, David Meyerholz, Michael Welsh
University of Iowa, Iowa City, IA

Background: The pancreas, liver and gallbladder are commonly involved in cystic fibrosis (CF) and the presence of acidic, dehydrated, and protein-rich secretions are characteristic findings. Pancreatic function studies in humans have been done by sampling the jejunal fluid. However, it has been difficult to separately study the function of pancreatic and biliary systems in humans with CF, because jejunal fluid contains a mixture of bile and pancreatic fluids. In contrast, pancreatic and biliary ducts open separately into the porcine intestine, therefore biliary and pancreatic fluid can be individually analyzed in CF pigs. Hypothesis: Pancreatic and biliary fluid secretion are both altered in CF pigs. Methods: We collected pancreatic and biliary fluid using a blind loop technique (4 wild-type (WT), 5 CF piglets) at baseline and 30 min after secretin (0.2 µg/kg IV). pH, volume and protein concentrations
were measured. For gallbladder pH studies, separate animals were used (8 WT, 12 CF piglets). The pancreatic localization of cystic fibrosis transmembrane conductance regulator (CFTR) was done with immunofluorescence. Pancreatic tissue enzyme expression was measured with activity assays and immunoblot. Results: CF pigs had pancreatic disease at birth, similar to those in humans. Pancreatic enzyme expression was significantly decreased in CF pigs compared to WT. We detected CFTR immunostaining in ducts and ductules of WT, not CFTR-/- piglets. The volume and pH of pancreatic fluid were significantly lower and protein concentration was >5-fold higher in CF. Secretin stimulation increased pancreatic fluid volume and pH in WT pigs, but not in CF. Baseline bile volume did not differ between WT and CF, but volume did not increase in response to secretin in CF. The bile pH was lower and protein concentration was 2-fold higher in CF. Conclusion: The pancreatic and biliary secretions are both altered in CF. Abnormal pancreatic and biliary secretion in CF may have important implications in disease pathogenesis.

32 NUTRITIONAL MANAGEMENT OF PEDIATRIC ACUTE PANCREATITIS. Soma Kumar, Wallace Crandall, Cheryl Gariepy, Nationwide Children's Hospital, Columbus, OH

The incidence of acute pancreatitis (AP) is increasing in the pediatric population and there is little literature on the management of AP in children, especially with regards to nutrition. The aim of this study was to describe the nutritional management of pediatric patients with AP and identify factors associated with the initiation of parenteral nutrition (PN).

Methods: We performed a retrospective chart review of 305 admissions with a discharge diagnosis of pancreatitis between Jan 2009 and Sept 2010. The diagnosis/severity of AP was determined using the Atlanta criteria. Demographic, laboratory and radiographic data were collected along with data regarding nutritional management. Univariate analysis was used to determine factors associated with PN use.

Results: 165 admissions met the definition for AP (150 mild, 15 severe) and were included. The average age was 11.4 yrs. 96.4% were initially fasted and the average fasting time for mild and severe patients was 58 hours and 157 hours, respectively (p=0.0001). The majority of patients were initially given a clear liquid diet (68%), and the rates of intolerance were similar (20-36.4%) despite type of nutrition given. The number of hours fasting also did not affect tolerance. 28 patients (18.5%) received PN. Of these, only 8 were started on PN after failing other methods of nutrition. PN use was positively associated with severe disease, discharge from a surgical service and traumatic etiologies while overweight/obese patients and idiopathic etiologies had less PN usage (p<0.05).

Conclusions: Nutritional management of pediatric AP differs when compared to adult guidelines. Pediatric patients with severe AP are fasted for extended periods despite evidence in adults demonstrating improved outcomes with early nutrition. Also, PN is used more frequently and earlier despite recent adult guidelines suggesting PN only be used when oral and enteral nutrition fail. It also appears that the type and timing of nutrition does not affect tolerance suggesting that greater consideration be given to early nutrition in the management of pediatric AP.

33 EFFECT OF EARLY AGGRESSIVE NUTRITIONAL MANAGEMENT IN PANCREATIC INSUFFICIENT CYSTIC FIBROSIS INFANTS DIAGNOSED BY NEWBORN SCREEN ON WEIGHT FOR LENGTH PERCENTILES & CLINICAL OUTCOME. Ruba Abdelhadi1,2, Brittany Pearo1,2, Lisa Matasovsky1,2, Donna Beth Willey Courand1,2,1. University of Texas Health Science Center, San Antonio, TX; 2. Christus Santa Rosa Cystic Fibrosis Center, San Antonio, TX

BACKGROUND: Adequacy of Cystic Fibrosis (CF) patients' nutritional status is directly related to better lung function & survival as mortality primarily results from cardiopulmonary complications. Infants born after implementation of CF newborn screen (NBS) have the advantage of early diagnosis & aggressive nutritional management and thus better clinical outcome & survival.

OBJECTIVES: To investigate the effect of early aggressive nutritional therapy in infants diagnosed with CF by NBS on their weight for length percentiles & clinical outcome & quality of life.

METHODS: A prospective longitudinal study at a single pediatric Cystic Fibrosis center evaluates weight for length percentiles among newborns with positive NBS for CF in whom we initiated high calorie fortified formula nutritional therapy in comparison to those born before implementation of CF NBS & were diagnosed later in life. Babies' weight for length percentiles were plotted at monthly intervals with surveillance of throat bacterial colonization. We monitor additional parameters: CF pulmonary exacerbations & hospitalization rates, fat-soluble vitamin levels, pulmonary function & FEV1, school performance & attendance & quality of life in each group.

RESULTS: 16 infants in (NBS group), diagnosed at 3 ± 1 weeks of age, all pancreatic insufficient. 19 infants in (non-NBS group), diagnosis after age 6 months, all pancreatic insufficient. Early aggressive high calorie fortified nutrition to NBS group resulted in significant acceleration of weight for length to above 50th percentile.

CONCLUSIONS & NEXT STEPS: Cystic fibrosis newborn screen has made it possible for early aggressive nutritional management which positively affects weight for length percentiles compared to children diagnosed later in life. To further determine the impact of early aggressive nutritional management on clinical outcomes, the prospective study will assess each group's nutritional status & BMI, pulmonary function & FEV1, rate of CF pulmonary exacerbation & hospitalization, age of Pseudomonas colonization, school performance & attendance & quality of life.
34 STATUS AND PREDICTORS OF FOLIC ACID AND B6 IN CHILDREN WITH CYSTIC FIBROSIS & PANCREATIC INSUFFICIENCY. Asim Maqbool, Joan I. Schall, Maria R. Mascarenhas, Norma E. Latham, Virginia A. Stallings, GI, CHOP, Philadelphia, PA

**Background:** Folic acid and vitamin B6 are involved in 1-methyl metabolism; status determinants of these B vitamins have not been well described in children with CF. **Objective:** To describe plasma B6 and RBC folate status & predictors in a current cohort of children with CF & PI following current clinical care practices. **Methods:** Baseline measurements were obtained from subjects (aged 5-17 yrs) with FEV1 > 40% predicted and no known liver or metabolic disease participating in a multicenter nutrition intervention study. RBC folate was analyzed from fasting whole blood samples by immunoassay and plasma B6 by HPLC. Dietary B vitamin intake from 3-day weighed food records and supplemental B vitamin intakes were reported. Daily B vitamin intakes were compared to DRI and expressed as %RDA. Descriptive statistics (medians, ranges) are presented for B6, folate, dietary and supplemental vitamin intakes. Predictors of plasma B6 & RBC folate including age, gender, dietary & supplemental B vitamins as both actual intake & %RDA were explored in multiple regression models. **Results:** 85% of the subjects had B6 levels within and 15% > reference range; 94% of the subjects had folate levels within, 2% > and 45% < the reference range. The best predictors of B6 status were dietary & supplement-based intake (R²=0.11, p=0.006); dietary folate intake was the best predictor of folate status (R²=0.09, p=0.02). Age & gender did not predict either B vitamin status. **Conclusions:** B6 & folate deficiency are uncommon in children with CF under current care models. Dietary intake is most important predictor of serum status both vitamins; supplement-based intake also predicts B6 status. Supported by NIDDK (R44DK060302), CTRC (UL1RR024134), the Nutrition Center at the Children's Hospital of Philadelphia, and Avanti Polar Lipids, Inc.

<table>
<thead>
<tr>
<th>Subjects, N, sex, age (mean±SD)</th>
<th>B6</th>
<th>RBC folate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration, μg/mL; median[range]</td>
<td>17.1 [5.1-91.7]</td>
<td>494 [231-1045]</td>
</tr>
<tr>
<td>Dietary intake, μg/d; median[range]; (%RDA)</td>
<td>1.9 [0.5-8.8]; (217; 51-931%)</td>
<td>416 [140-1472]; (159;39-491%)</td>
</tr>
<tr>
<td>Supplement-based intake, μg/d; median[range]; (%RDA)</td>
<td>2.4 [0-75]; (311; 0-7500%)</td>
<td>400 [0-1200]; (100; 0-400%)</td>
</tr>
</tbody>
</table>

35 EPIDEMIOLOGY OF ACUTE PANCREATITIS IN HOSPITALIZED CHILDREN IN THE UNITED STATES FROM 2000 TO 2009. Chaitanya Pant³, Michael P. Anderson³, Anas Bitar³, Abhishek Deshpande², Marilyn I. Steele³, Thomas J. Sferra¹,².1UH Rainbow Babies & Children’s Hospital, Cleveland, OH; ²CWRU School of Medicine, Cleveland, OH; ³University of Oklahoma HSC, Oklahoma City, OK

**Background:** Several recent single-center studies suggest an increasing incidence of acute pancreatitis (AP) in children. **Objectives:** To evaluate trends in hospitalization rates (incidence) and outcomes for AP in children at a U.S. national level. **Methods:** We used the U.S. Healthcare Cost and Utilization Project Kids' Inpatient Database for the years 2000-2009. Data were weighted to generate national-level estimates. Hospitalization rates are expressed as AP hospitalizations per 10,000 pediatric hospitalizations per year. Data were evaluated by Cochrane-Armitage test (for trend analyses), and univariate and multiple regression analyses. Case-control matching using high-dimensional propensity scores was performed in a 1:5 ratio (with and without AP) to evaluate outcomes. **Results:** We identified 54,980 cases of AP. From 2000 to 2009, the hospitalization rate for a principal diagnosis of AP increased from 23.1 to 34.9 (P<0.001) and for all-diagnoses 38.7 to 61.1 (P<0.001). There was an increasing trend in the incidence of principal and all-diagnoses of AP (P<0.001); this occurred in all age groups (5-yr increments after 1 yr of age). AP hospitalization rates were highest in the 11-15-yr (48.3 principal; 77.6 all-diagnoses) and 16-20-yr (44.5 principal diagnosis; 80.0 all-diagnoses) age groups; lowest rates were in the 1-5-yr age group (8.2 principal; 16.8 all-diagnoses). Mortality decreased (13.1 to 7.6 per 1,000 cases, P<0.001), median length of hospital stay (LOS) decreased (5 to 4 days, P<0.001), and median charges increased ($14,977 to $22,663, P<0.001). Case-control matching demonstrated lower risk of death (OR 0.82, 95% CI, 0.74-0.92), longer LOS (OR 2.47, 95% CI, 2.42-2.52), and higher charges (OR 1.59, 95% CI, 1.55-1.62) in those with AP. **Conclusions:** These results: (i) demonstrate a rising incidence of AP in hospitalized children, however mortality decreased, during the years 2000 to 2009 and (ii) contribute to a better understanding of pediatric AP.
36 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PEDIATRIC PATIENTS. Matthew J. Giefer¹, Richard Kozarek²,¹, ªSeattle Children’s, Seattle, WA; ²Virginia Mason Medical Center, Seattle, WA

Endoscopic retrograde cholangiopancreatography (ERCP) is a diagnostic and often therapeutic procedure which can be performed for multiple pancreaticobiliary diseases. There is a large body of literature demonstrating the safety and efficacy of ERCP in adults and the procedure has been successfully performed in the pediatric population; however, the data relating to this application has been generally restricted to case reports and small case series. In this study, a retrospective analysis was performed on patients ≤ 18 years who underwent ERCP since 1994 at either Seattle Children's Hospital or Virginia Mason Medical Center. Subjects were identified from diagnosis and billing codes. A total of 426 procedures were identified and the medical record was examined to record patient age, indication for ERCP, procedural findings, therapeutic interventions preformed, and procedural complications. Detailed information was available for 335 patients. Chronic/recurrent pancreatitis was the most common indication for pediatric ERCP and was the primary indication for the procedure in 39% of the cases. Biliary tract disease was the second leading indication at 33%. Therapeutic interventions were common and occurred in 79% of cases. There was a low incidence of technical failure (3.9%). No deaths occurred and the overall procedural complication rate was 11.3%. Post-ERCP pancreatitis was the most frequent complication and was observed in 7.5% of patients with most cases being of mild or moderate severity. This study is larger than any published pediatric ERCP report and suggests that although the indications for the procedure are unique from those in adults, it can be safely and successfully preformed in the pediatric population.

37 SAFETY OF SECRETIN ADMINISTRATION IN CHILDREN. Beth Loveridge Lenza¹, Karoly Horvath², Zhaoping He², Randolph Brenn², Pediatric Gastroenterology, K. Hovnanian Hospital for Children, Jersey Shore University Medical Center, Neptune, NJ; ²Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL; ³AI duPont Hospital for Children, Wilmington, DE

Aim. The aim of the study was to compare the anesthesia records of children (0-18 years) who underwent procedures with and without secretin pancreatic function tests (sPFT) with or without secretin was performed or the patients had combined procedure (e.g. bronchoscopy, ENT surgery etc).

Methods. The electronic anesthesia database was searched and all the recorded parameters were saved into an excel spreadsheet for analysis. In addition to the two groups a subgroup analysis was performed based on that only EGD procedures and it was in average 7/min higher in the secretin group. There were mild elevations on the systolic and diastolic blood pressures. None of these changes were clinically significant between the main and subgroups. There was no any complication reported during the anesthesia and procedures and post-procedure period.

Conclusions. Secretin PFT is a safe procedure. It only slightly prolongs the total procedure and anesthesia time. There were no clinically significant changes in the vital parameters in the secretin group and there was no side effect recorded.

38 CYSTIC FIBROSIS TRANSMEMBRANE REGULATOR KNOCKOUT MICE EXHIBIT ABERRANT GASTROINTESTINAL MICROBIOTA. Yvette K. Wild¹, Katherine C. Goldfarb¹, Robert De Lisle², Weidong Kong², Eoin L. Brodie¹, Susan V. Lynch¹, Pediatric Gastroenterology, Hepatology and Nutrition, University of California - San Francisco, San Francisco, CA; ²Medicine, University of California - San Francisco, San Francisco, CA; ³Ecology, Berkeley National Laboratory, Berkeley, CA; ⁴Anatomy and Cell Biology, University of Kansas, Kansas City, KS

Introduction: Cystic fibrosis (CF) patients have aberrant gastrointestinal (GI) epithelial transport, excess mucus production, intestinal obstruction, small intestine bacterial overgrowth and slow GI transit. Though these findings likely reflect GI microbial shifts, the GI microbiome is understudied in CF. We compared GI microbiota in wild type (WT) and CFTR-deficient (CF) mice before and after antibiotics to determine if administering antibiotics improves the CF GI microbiome.

Methods: Four groups of mice [WT (n=3), WT+antibiotics (n=3), CF (n=3) and CF+antibiotics (n=3)] were analyzed for GI bacterial composition. Antibiotics were administered from weaning to 6 weeks of age. Small intestine contents were collected and extracted for total DNA. High-resolution phylogenetic microarray (PhyloChip) profiled microbiota. Statistical analyses were in the R environment.

Results: Decreased community richness and diversity were seen in CF (p<0.05), who exhibited decreased abundance
of 305 taxa compared to WT (p<0.05), the majority belonging to the Proteobacteria phylum. CF mice showed increases in enrichment of 157 taxa belonging to the Mycobacteria, Pseudonocardia, Desulfovibrio and Sptreptomyces. Antibiotics resulted in compositional convergence of the CF and WT microbiota (p<0.003). In CF mice, antibiotics resulted in decreased relative abundance of the Enterobacteria in particular. Conclusion: GI bacterial colonization is impacted by CF, which likely impacts GI function and mucosal immune responses. Antibiotics restructure the GI community, with CF mice diversity increased coincident with a loss of the Enterobacteria, suggesting members of this family may repress community diversity in CF. Understanding the CF GI microbiome may reveal therapeutic strategies for this population.

39 NUTRITIONAL OUTCOME OF HEALTHY WEIGHT AND OBESITY CHILDREN WITH ACUTE PANCREATITIS MANAGED WITH ENTERAL NUTRITION. Carmen A. Sánchez-Ramírez1,3, Alfredo Larrosa-Haro3,2, Mariana Gómez-Najera2, Bojorquez Maria del Carmen2,3, Rocio Macías-Rosales2,3, Yolanda Castillo De León2, Osvaldo García-Salazar2-3, 1Facultad de Medicina, Universidad de Colima, Colima, Mexico; 2Pediatric Gastroenterology and Hepatology, UMAE, HP, IMSS, Guadalajara, Mexico; 3Instituto de Nutrición Humana, Universidad de Guadalajara, Guadalajara, Mexico

AIM: To compare the outcome of the nutritional status of healthy weight and obese children with acute pancreatitis (AP) managed with enteral nutrition

PATIENTS AND METHODS: Design: Clinical trial. Setting: A pediatric referral hospital. Sample= 17 children with AP, median age 144 months, 9 cases with necrotic-hemorrhagic AP. 12 females. Intervention: enteral nutrition. Outcome: nutritional status. All cases were managed with jejunal infusion of elemental formula, initial intake ~100%, target intake ~130% DRI, one week for edematous AP and two weeks for hemorrhagic AP. Nutritional status: z-scores of weight/height and adiposity arm anthropometrical indicators (triceps skinfold, arm fat area and arm fat index). Analysis: Friedman test.

RESULTS: 58.8% had healthy weight and 41.2% were overweight/obese. Intragroup comparison of weight/height and arm indicators in the healthy group children remained within -1 to +1 z-score limits. Intragroup comparison of the overweight/obese group showed a statistically significant decrease in z-score values in most cases from above 2SD to the limits -2 to +2 SD.

CONCLUSIONS: The outcome of body composition in children with AP managed with a similar enteral nutrition protocol is different in children with healthy weight than in overweight/obese patients. Progressive and significant loss of fat deposits in the overweight/obese group probably underlines a different metabolic response to a severe organic insult as AP.

40 OVERWEIGHT AND OBESE CHILDREN HAVE A DIFFERENT SERUM BIOCHEMISTRY AND BLOOD CELL PROFILE THAN HEALTHY WEIGHT CHILDREN WITH ACUTE PANCREATITIS. Mariana Gómez-Najera2, Carmen A. Sánchez-Ramírez2, Alfredo Larrosa-Haro2,1, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatría, CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

AIM: To compare biochemical and hematological data of healthy weight versus overweight or obese children with acute pancreatitis (AP).

PATIENTS AND METHODS: Design: Cohort, two-week follow-up of obese and healthy weight children with AP. Setting: A pediatric referral hospital. Independent variable: nutritional status. Dependent variable: biochemical and hematological data. Patients: 17 pediatric patients with AP, 9 with healthy weight and 8 with overweight or obesity, mean age 126.5 months, 11 females, 52.9% with hemorrhagic AP. Protocol: Biochemical and hematological data were recorded on admission and at days 3, 7 and 14. Analyses: Friedman test for Intragroup and with Kruskal-Wallis for intergroup comparisons.

RESULTS: Amylase, lipase and liver function test (transferases, GGT, bilirubin, and alkaline phosphatase) had no statistical differences along the trial. Both groups had a progressive and significant decline of hematocrit. On admission, CRP was increased in both groups, higher in the obese; this inflammation marker returned to normal in healthy weight patients and remained high in the obese group. Albumin was <3g/dL in both groups and admission and remained low in the obese children along the trial. Serum glucose, calcium and chloride had significant concentration changes in the obese group along the study.

CONCLUSIONS: Obese children with AP had a different adaptive response to the disease than healthy weight: inflammation response, albumin, glucose and electrolyte levels were impaired. This condition may constitute a disadvantage of obese children in dealing with an AP episode.
41 ACUTE NECROTIZING PANCREATITIS IN CHILDREN. Aileen Raizner\textsuperscript{1}, Uma P. Phatak\textsuperscript{1}, Kenneth Baker\textsuperscript{1}, Mohini G. Patel\textsuperscript{1}, Sohail Z. Husain\textsuperscript{1}, Dinesh S. Pushankar\textsuperscript{1}, \textsuperscript{1}Pediatric Gastroenterology, Yale University, New Haven, CT; \textsuperscript{2}Radiology, Yale University, New Haven, CT; \textsuperscript{3}Pediatric Gastroenterology, University of Pittsburgh, Pittsburgh, PA

Objective: Necrotizing pancreatitis (NP) is a rare occurrence in children. We report the etiologic factors, course and outcomes of acute NP in children.

Methods: We performed a retrospective study of children with NP diagnosed over the last 21 years at our hospital. Strict CT scan criteria were used to diagnose NP and to determine the severity index (the sum of inflammation grade and necrosis score). Results: Eight children (4 boys) were diagnosed with NP and had a variable etiology (Table). All had significant elevation of amylase and lipase (> 3 times the upper limit of normal) and severe pancreatic necrosis on CT scan. Leucocytosis, hypoalbuminemia and hypocalcimia were seen in the majority of patients. All had a prolonged hospitalization (range 9 to 40 days) and 5 patients required ICU admission. Patients developed various acute systemic complications during the hospital stay and 75% developed late complications (Table). The CT scan severity index correlated with the risk of complications. All patients responded to aggressive medical therapy and none required surgical intervention. Pseudocysts resolved spontaneously in all patients. Patient 4 developed severe pancreatic atrophy and requires insulin and pancreatic enzyme therapy. There were no deaths attributable to NP. Conclusions: Acute NP has a variable etiology in children. CT scan is useful for the diagnosis and assessment of severity. NP in children is associated with severe acute and late complications and requires aggressive supportive care and close follow up.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Etiology</th>
<th>Acute complications</th>
<th>Late Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.9</td>
<td>Minocycline</td>
<td>Circulatory failure, Pleural effusion, Ascites, Splenic vein thrombosis</td>
<td>Transient hyperglycemia</td>
</tr>
<tr>
<td>2</td>
<td>17.4</td>
<td>Gallstones</td>
<td>Atelectasis</td>
<td>Pseudocyst</td>
</tr>
<tr>
<td>3</td>
<td>13.8</td>
<td>Diabetes</td>
<td>Atelectasis</td>
<td>Pseudocyst</td>
</tr>
<tr>
<td>4</td>
<td>11.5</td>
<td>Asparaginase</td>
<td>Bilateral pleural effusions, Ascites, Oligouria, Hyperglycemia</td>
<td>Pseudocyst, Diabetes, Exocrine insufficiency</td>
</tr>
<tr>
<td>5</td>
<td>4.1</td>
<td>Unclear</td>
<td>Oligouria, Hyperglycemia</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>Valproate</td>
<td>Bilateral pleural effusion, Ascites, DIC</td>
<td>Nil</td>
</tr>
<tr>
<td>7</td>
<td>17.8</td>
<td>Asparaginase</td>
<td>Bilateral pleural effusion, Hyperglycemia, Ascites, DIC</td>
<td>Transient hyperglycemia</td>
</tr>
<tr>
<td>8</td>
<td>20.7</td>
<td>Alcohol</td>
<td>Bilateral pleural effusion, Ascites</td>
<td>Pseudocyst</td>
</tr>
</tbody>
</table>

42 PATIENT RISK FACTORS FOR ACUTE PANCREATITIS ASSOCIATED WITH HOSPITALIZATION IN CHILDREN. Amit S. Grover, Amanda J. Deutsch, Menno Verhave, Jenifer R. Lightdale Gastroenterology, Boston Children's Hospital, Boston, MA

Little is known about pediatric co-morbidities that may impact hospitalization for acute pancreatitis (AP). One question has been whether increased body mass index (BMI) may be a risk factor. AIM: The aim of our study was to identify co-morbid conditions, including overweight/obesity that may affect hospitalization of children with acute pancreatitis. METHODS: We performed a retrospective chart review of all children presenting with or developing AP (search ICD-9 code 577.0) at Boston Children's Hospital between 1/1/10- 12/31/10. The diagnosis was manually confirmed by review of records, labs and imaging. Patients with multi-organ failure were excluded. Our primary outcome was length of stay (LOS) after diagnosis. Data extraction included anthropometrics. RESULTS: 57 patients (26 (46%) male; median age 14 years (IQR 8-17)) were evaluated. 7 (12%) had >1 admission during the study period. 40 (70%) had pancreatitis as the admitting diagnosis; AP was diagnosed at a median of hospital day 4 (IQR: 2, 6) in those admitted for other indications. Median amylase at diagnosis was 342 unit/L (IQR: 167, 714); median lipase 910 unit/L (305, 1443). The most common suspected etiology was medication (n=20 (37%): including antibiotics (45%); anti-epileptics (20%) and chemotherapeutics (20%), followed by idioopathic 10 (18.5%). 7 (13%) had gallstone disease. 13 (23%) patients had psychiatric diagnoses, including ADHD (54%) and mood disorder (46%). 10 (18%) had seizure disorders and 6 (11%) cancer. 18 (35%) patients had a BMI > 85% at time of diagnosis. Median length of stay (LOS) for all patients was 7 days (IQR 3, 13 days), with a range of 0-135 days. Patients who were overweight/obese had a longer LOS than those who were normal- or underweight (median 9 (IQR 5.3-31) vs 7 (3-11.8) days, p=0.08). DISCUSSION: A greater understanding of patient risk factors is important to understanding factors which may impact hospitalizations for acute pancreatitis in children. Larger, multi-center studies are needed to investigate whether increased BMI may be associated with longer hospitalizations.
43 EFFECT OF GASTROSTOMY TUBE PLACEMENT ON HOSPITALIZATION RATE OF CHILDREN WITH PANCREATIC INSUFFICIENT CYSTIC FIBROSIS. Ruba Abdelhadi1,2, Brittany Pearo1,2, Lisa Matasovsky1,2, Donna Beth Willey Courand1,2, 1Pediatrics, University of Texas Health Science Center at San Antonio, San Antonio, TX; 2Christus Santa Rosa Children’s Hospital Cystic Fibrosis Center, San Antonio, TX

BACKGROUND: Pancreatic insufficient Cystic Fibrosis children present a serious nutritional challenge to the multidisciplinary team of clinicians, particularly if they sustained neonatal surgical emergency resulting in short bowel. Maintenance of BMI above the 50th percentile is a strong predictor of better lung function & improved survival. Gastrostomy tube placement provide a practical method of enteral renourishment that may positively impact clinical outcome. OBJECTIVES: To investigate the effect of gastrostomy tube placement & enteral renourishment on CF lung exacerbations & hospitalization rates. METHODS: A prospective study at a single pediatric Cystic Fibrosis center compared hospitalization rates in pancreatic insufficient CF patients who have received enteral renourishment via gastrostomy with a non-gastrostomy pancreatic insufficient CF group that is matched in age and lung disease severity between 2007 and 2012. The following data were collected: demographics, age of gastrostomy placement, number of hospitalizations related to CF related lung disease exacerbations, FEV1.

RESULTS: 7 patients underwent gastrostomy tube placement & Nissen FP for failure to thrive and weights for lengths below 50th percentile for age and GERD. The mean age 21 ± 11 months. 38 patients in the control group received high calorie oral supplements without gastrostomy placement. The hospitalization rate among the two groups was 5 ± 3 hospitalizations per year. CONCLUSIONS: Cystic fibrosis related lung disease and exacerbations necessitating hospitalization & IV antibiotic therapy have not been positively affected by gastrostomy placement and aggressive enteral renourishment. While nutrition plays a vital role in lung function, other multiple factors impact lung function and CF exacerbation including but not limited to compliance to medical management and proper chest PT.

44 JOHANSON-BLIZZARD SYNDROME: EXPANDING THE PHENOTYPE. Kate M. Ellery1,2, Steven H. Erdman1,2, 1Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Nationwide Children’s Hospital, Columbus, OH; 2The Ohio State University College of Medicine, Columbus, OH

Johanson-Blizzard Syndrome (JBS) (OMIM #243800) is a rare autosomal recessive disorder characterized by facial dysmorphic features, ectodermal abnormalities, obligatory exocrine pancreatic insufficiency and early childhood growth failure. Most patients are diagnosed by clinical criteria prenatally or in early infancy. JBS is typically due to nonsense, frame shift and splice-site mutations of the UBR1 gene leading to absence of the UBR1 protein. We describe identical twin brothers with delayed presentation and mild phenotypes. As infants, they were diagnosed with ectodermal dysplasia based on nail, hair and dental findings. Our Division has followed Twin B since age 13 years for cyclic vomiting syndrome. At age 15 years he developed sudden onset "oily" diarrhea (10-15 stools/day) and an associated drop from the 86th to the 71st percentile for weight. Initial evaluation for gastrointestinal infection, celiac disease and inflammatory bowel disease was unremarkable. Nutritional screening documented fat-soluble vitamin deficiencies and fecal elastase level of 29.8 µgE1/g stool (normal >100 µgE1/g stool). Abdominal imaging revealed characteristic fatty replacement of the pancreas and pancreatic stimulation testing showed near absent digestive exocrine secretion. Subtle nasal alae malformation has been documented on exam. Pancreatic enzyme replacement therapy and fat-soluble vitamin supplementation resulted in significant weight gain. Twin A has refused medical evaluation. However, per maternal and Twin B report, he has a very thin body habitus with chronic diarrhea. Both brothers have declined genetic counseling/testing. The differing presentations of identical twins presenting beyond childhood illustrates the milder phenotype of this disorder. Alternate genetic mechanisms due to compound heterozygous mutations with missense mutations or in-frame deletions may allow for partial UBR1 function. The differing phenotypes of these twins suggest either environmental or epigenetic events as modifying factors.
been followed for at least 12 months on a GF diet were included. RESULTS: 172 pts (57M,115F) were screened. A total of 147 pts (51M,96F) mean age 9.5 yrs (range 0.8-17.9) met inclusion criteria. 54 pts (16M,38F) mean age 8.1 yrs (range 0.8-17.7) with GI symptoms were evaluated for response to a gluten free diet. Resolution was noted in 100% (13/13) of pts with abdominal distention/diarrhea/FTT, 82% (18/22) with abdominal pain alone, 80% (8/10) with vomiting, but only 11% (1/9) with constipation. 89% of pts with constipation continued to require laxatives. There were 93 pts (35M/58F) mean age 10.3 yrs (range 2.6-17.9) with non-GI symptoms. Response was noted in 100% (3/3) of pts with anemia and 28% (8/28) with short stature. CONCLUSIONS: CD pts presenting with abdominal distention ± diarrhea, abdominal pain alone, vomiting, or anemia demonstrate excellent rates of response to a GF diet. However, there were low rates of response to the diet in CD pts presenting with constipation or short stature. This suggests that the diagnosis of CD in many of the pts presenting with constipation or short stature is serendipitous and not associated with the presenting complaint.

52* THE NEW ESPGHAN GUIDELINES FOR CELIAC DISEASE: HOW MANY BIOPSIES CAN WE REALLY SKIP? Catherine D. Newland, NurAlima Grandison, Stefano Guandalini, Pediatric Gastroenterology, University of Chicago, Chicago, IL

Background: The diagnostic criteria for celiac disease (CD) were recently reviewed and a new set of guidelines published by ESPGHAN in January of 2012. The aims of this study were: 1) to retrospectively determine how many patients would avoid the biopsy; and 2) to verify potential drawbacks in eliminating endoscopy.

Methods: A retrospective chart review was performed on pediatric patients enrolled in the University of Chicago Celiac Database from August 2008 to May 2012. Information was collected on patients with a diagnosis of CD including: gender, date of birth, date of diagnosis, endoscopic pathology findings, and celiac serologies.

Results: A total of 332 records of pediatric CD patients were reviewed. Among them, 150 symptomatic patients (98 females) had data available for both tissue transglutaminase IgA (tTG IgA) and endomysial antibodies (EMA) at presentation. Average age at diagnosis was 9.1 years. Seventy patients (47%) had tTG greater than 10 times the upper limit of normal and a positive EMA. Of these 70 patients, 59 (84%) underwent endoscopy with biopsies with the distribution of Marsh scores as follows: Marsh 0 - 2 (3.5%), Marsh 1 - 4 (6.8%), Marsh 2 - 18 (30.5%), Marsh 3 - 35 (59%). Of interest, 6 (10%) of the biopsied patients had additional, unexpected diagnoses found on pathology including eosinophilic esophagitis (1), chronic gastritis (1), reflux esophagitis (3), reflux esophagitis and antral gastritis (1).

Conclusion: Almost half of the pediatric patients diagnosed with celiac disease in our series would have met the new ESPGHAN criteria allowing to forgo duodenal biopsy. However, by avoiding the diagnostic procedure, additional, unexpected diagnoses would have been missed in as many as 10% of such patients.

53 EARLY UNIVERSAL SCREENING FOR ASYMPTOMATIC CELIAC DISEASE PREVENTS OSTEOPOROSIS AND BONE FRACTURES: A COST-EFFECTIVENESS ANALYSIS

K. T. Park, Raymond Tsai, Louise Wang, Nasim Khavari, Laura Bachrach, Dorsey Bass, Stanford University / Lucile Packard Children’s Hospital, Palo Alto, CA

Patients with asymptomatic or poorly managed celiac disease (CD) can develop osteoporosis, leading to peripheral and vertebral fractures, preventable by a gluten-free diet. Current clinical practice may result in undiagnosed CD with the consequence of otherwise preventable osteoporosis and fractures. AIM: The aim of our analysis is to determine the cost-effectiveness of Universal Screening (US) versus Standard Practice (SP) strategies for CD screening, given the risk of future bone disease if untreated. METHOD: We developed a lifetime Markov Model, each with a cohort of 10,000 patients at 12 years of age when 2 screening strategies begin. Model was stratified by gender to capture differential gender risk for bone disease. Serological levels of TTG IgA and total IgA are used for screening with mucosal biopsies for confirmation. Transition probabilities and quality of life estimates were obtained from literature. Generalizable cost estimates and Medicare reimbursement rates were used. Deterministic and probabilistic sensitivity analyses were run. RESULT: In females, average life-time costs were $23,566 and $23,462 for US and SP strategies, respectively, corresponding to average QALY-gained of 25.63 and 25.62. This represents an ICER of $10,770 for US and SP strategies, corresponding to QALY-gained of 25.61 and 25.95 - making universal screening in females not cost-effective. In contrast, among males, the costs were $10,766 and $10,731.61/QALY-gained for the US strategy. Deterministic and probabilistic sensitivity analyses showed that the model was robust to realistic changes in all the variables in the model, and the cost-effectiveness of the US strategy was not sensitive to any single variable in the model. CONCLUSION: Universal serologic screening for CD is cost-effective for all males at age 12. Early diagnosis of asymptomatic CD and subsequent treatment with strict GFD will prevent silent bone loss and future hip and vertebral fractures, increasing overall quality of life and decreasing healthcare costs.
54 CD4/CD8 LYMPHOCYTE SUBPOPULATIONS DENSITY IN THE DUODENUM OF CHILDREN WITH CELIAC DISEASE. Elizabeth Arce-Mojica1, Rocio Macias-Rosales1, Alfredo Larrosa-Haro2
1Gastroenterology and Nutrition, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Centro Universitario en Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

AIM: To compare the density of CD4/CD8 lymphocyte subpopulations, morphology and inflammatory activity in duodenal biopsies of children with celiac disease (CD) versus healthy controls (HC).

PATIENTS AND METHODS: Biopsies of 8 children with CD and 10 HC, studied at a referral hospital from 2001-2011, were reviewed. Duodenal morphology, inflammatory activity and CD4/CD8 lymphocyte subpopulations were compared between the study groups. Histological analysis was performed with and ad hoc semi-quantitative protocol validated in previous studies. This type of histological analysis permitted the use of statistic test as chi square, Fisher and Mann-Whitney U tests.

RESULTS: Five CD patients were girls. The age of onset of symptoms was 9 months and the age at diagnosis was 18 months. At diagnosis, 2 patients had iron deficiency anemia and all had albumin <3g/dL and impaired one-hour d-xylose absorption (<20mg/dL). Anti-endomysium and anti-gliadin IgA antibodies were identified in 4 out of 6 CD patients. All CD patients had small bowel villous atrophy, brush border disruption and crypt lymphoid aggregates. Five patients had impaired weight/height and 3 height/age. CD8 density was higher in CD.

CONCLUSIONS: CD prevalence seems to be low in Mexico, although it may not be searched properly. Morphology and inflammation picture was similar to other pediatric series. Presence of CD8 lymphocyte subset in contrast to controls suggest that CD induces its proliferative activation.

55 CHILDHOOD CELIAC DISEASE, EXPERIENCE OF A SINGLE PRIVATE CENTER IN SAUDI ARABIA. Asaad Assiri, Anjum Saeed, Pediatrics, King Khalid University, Hospital, King Saud University, Riyadh, Saudi Arabia

Introduction: Celiac disease (CD) or gluten sensitive enteropathy is an autoimmune disorder caused by permanent sensitivity to ingested gluten in genetically susceptible individuals.

Objective: To report our experience of pediatric CD, trend of presentation from a single private center in the central region of Saudi Arabia.

Design & setting: Collection of clinical cases, hospital based.

Patients & methods: We report children between ages of 0.5-18 years with classical and non-classical presentation of celiac disease and children at high risk like celiac sibs, IDDM or other autoimmune diseases over a period of 4 years (Jan 2008-Dec 2011). The diagnosis of celiac disease was made on the basis of clinical history, physical examination, serological markers and small bowel biopsies.

Results: On analysis of the records we identified a total of 124 patients with confirmed CD. Out of 124 patients, 68 (54.84%) were male. Their mean age was 10.3 years (range 0.5-18 years). Non-classical manifestations were documented in 31 (91.1%) patients and histopathology showed marsh grade B1/type 3 in 30 patients (88.2%), grade B1/type 2 patients in 3 (8.82%) and one patient had grade A/type 1.

Conclusion: Classical malabsorption of CD usually presents in early childhood but atypical presentation is more common in young children and adolescent. Pediatrician should think of CD as a diagnosis in any child with atypical presentation.

56 PATTERN OF GLUTEN SENSITIVE ENTEROPATHY, EXPERIENCE OF TWO MAJOR CENTERS FROM CENTRAL REGION SAUDI ARABIA. Asaad Assiri, Anjum Saeed, Ahmed Alsarkhy, Mohammad Elmouzan, Yassin Haamid, Moona Alasmi, Pediatrics, King Saud University, Riyadh, Saudi Arabia

Introduction: Celiac disease (CD) is an immune-mediated disorder that affects primarily the gastrointestinal tract due to ingested gluten in genetically predisposed individuals.

Objective: To report pattern of pediatric celiac disease from central region of Saudi Arabia.

Design and settings: Collection of clinical cases, hospital based.

Patients and methods: The data of children diagnosed as CD from two major centers, was analyzed from Jan 2000 to Dec 2011. Children between the ages of 0.5-18 years were included. The diagnosis of CD was based on clinical presentation, physical examination and confirmed by serological markers with small bowel biopsies.

Results: On analysis of the records we identified a total of 124 patients with confirmed CD. Out of 124 patients, 68 (54.84%) were male. Their mean age was 10.3 years (range 0.5-18 years). Non-classical manifestations were found in 60 (48.3%) patients with isolated short stature in forty one (33.0%), unexplained rickets in 11 (8.8%), resistant iron deficiency anemia in 6 (4.83%). On screening, 18 (14.5%) IDDM children had CD, 7 (5.64%) children were picked on sibs screening and 3 (2.41%) were with down syndrome. GI symptoms were present in 41 (33.0%) patients with abdominal pain and distension in 30 (24.1%) and chronic diarrhea was present in 11 (8.87%) patients.
Growth parameters showed weight and height were below 3rd centile in 75 (60.4%) patients. Celiac serology was positive in 119 (95.9%) patients. Small bowel histopathology showed marsh grade B1/type 3 in 96 patients (77.4%), grade B1/type 2 in 25 (20.1%) and 3 patients (2.41%) had grade A/type 1.

Conclusion: Trend of non classical presentation prevails with increasing age in children and adolescent celiac disease.

Key Words: Celiac disease, non-classical manifestations

57 EVALUATION OF HEMATOLOGIC STATUS (HS) IN CHILDREN WITH INITIAL DIAGNOSIS OF CELIAC DISEASE (CD). Christian G. Boggio Marzet, Mónica Ballagán Lucero, María Anabel Telli, Min Chung Ko, Cecilia Tennina, Pediatric Gastroenterology & Nutrition Section, Hospital "Dr.I.Pirovano", Capital Federal, Argentina

Introduction: Hematologic manifestations are frequent in CD because it is a multisystemic disorder, being anemia the most common blood disorder in new cases of CD.

Objective: To assess HS of patients at diagnosis of CD.

Material and Methods: Sample of 53 patients with initial diagnosis of CD who attended at the Pediatric Gastroenterology Section in Hospital Pirovano during the period 01-01-2001 to 31-12-2010. Z scores were estimated for weight, height and BMI according to WHO references adapted by the Argentine Ministry of Health. The HS was assessed according to the consensus of the National Committee of Hematology from the Argentine Pediatric Society.

Results: 60.4% male. Mean age 7.89 years (2.11-16.76) and divided into two age groups: Group A (GA): 2-9 years and Group B (GB): 9 to 16 years. The overall prevalence of iron deficiency anemia at diagnosis was 30%, without statistically significant differences between the two groups (Fisher p = 0.883). The severity of anemia according to age group showed mild anemia (56% GA vs 12.5% GB) and moderate to severe (12.5% GA vs 19% GB) (Fisher p = 0.245). The relationship between anemia and weight and height z-scores for age showed statistically significant association between children with standard z-score (9%) vs z-score below normal (21%) (Fisher p = 0.019).

Conclusions: Anemia is the most frequent hematological alteration at diagnosis of CD appearing not to be associated the severity with age. There was a relationship between the degree of impaired growth profile and the presence of anemia that could be due to the lack of early diagnosis.

58 TO DETERMINE THE PREVALENCE OF ANTI-TISSUE TRANSGLUTAMINASE ANTIBODIES IN CHILDREN WITH AUTISM SPECTRUM DISORDERS (ASD)

Prita Mohanty1, Jessica Roesser2, Tristram Smith2, Marilyn Brown1, Susan Hyman2, Pediatric Gastroenterology, University of Rochester Medical Center, Rochester, NY; 2Neurodevelopmental and Behavioral Pediatrics, University of Rochester Medical Center, Rochester, NY

Background and Aims: An association between Autism and Celiac Disease has been reported. Despite the paucity of scientific support to date, screening for celiac disease in children with Autism has been recommended by some, even in the absence of gastrointestinal symptoms. Because of the variable presentation of Celiac disease with GI and non-GI symptoms, it is important to determine if children with ASD, who often cannot report symptoms, are at increased risk. If so, then there would be support for both routine screening for Celiac disease and recommendation of a gluten free diet (GFD). The purpose of our study was to determine if children with Autism have an increased risk for Celiac disease.

Specific Aim: The aim of the study was to determine the prevalence of Anti-tissue Transglutaminase (tTG) antibodies in children with Autism Spectrum Disorders.

Methods: Retrospective chart review of 1568 patients with ASD seen through a regional developmental assessment clinic over two years, identified 149 children between 2 -18 years of age who had testing for tTG antibodies. Results: Four children with ASD (2.7%) had positive celiac antibodies. Small bowel biopsies were performed in 2 out of the 4 children and were negative for Celiac disease. In the other 2 children, parents reported clinical improvement on a GFD. The most common indications for celiac screening in ASD were constipation (32 %), diarrhea (13 %) and prior to starting the GFD (13 %). A GFD was trialed in 24 % of patients, of which 37 % reported subjective improvement in behavior and 21 % had improvement in GI symptoms.

Conclusion: The prevalence of celiac antibodies in ASD was found to be the same as in the general population. No increased association of celiac disease and ASD was demonstrated, although subjective benefit from a GFD was anecdotally reported by families.

59 REVISED CELIAC DISEASE DIAGNOSIS GUIDELINES: WILL WE OVER TREAT?

Marina Orsi, Federico Ussher, Laureana Olleta, Silvia Christensen, Carlos Lifschitz, Hospital italiano, Buenos Aires, Argentina

Objectives: Proposed ESPGHAN recommendations for diagnosing celiac disease (CD) suggest avoiding initial biopsy in symptomatic patients whose tissue transglutaminase IgA (TTGA) is 10 times the upper limits of normal (ULN) or greater. The purpose of our study was to determine the positive predictive value (PPV) of TTGA in such
group of patients and compare the value with that with lower TTGA.

**Methods:** We reviewed the records of patients who underwent a small bowel biopsy for diagnosis of CD between July 2001 and May 2012. TTGA values and biopsy reports were recorded from medical records and the PPV of TTGA was calculated. The Marsh biopsy score was used as a gold standard.

**Results:** Two hundred and eleven patients underwent biopsy (age range 1 - 18 yrs.). PPV of TTGA among patients whose TTGA was less than 10 times the ULN (n=87) was 64.28% if symptomatic and 67.7% if asymptomatic. Among the 124 that had TTGA values 10 times the ULN or greater, 4 had a normal small bowel biopsy. PPV was 96.77%.

**Conclusion:** Although the suggested cutoff point for TTGA seems to improve substantially the PPV of the test for diagnosing CD, in our population 3.2% of patients would have been placed unnecessarily on a gluten free diet if the new ESPGHAN recommendations had been applied.

---

**ENDOSCOPY IN THE DIAGNOSIS OF INTESTINAL GRAFT-VERSUS-HOST DISEASE: IS LOWER ENDOSCOPY WITH BIOPIST AS EFFECTIVE IN DIAGNOSIS AS UPPER ENDOSCOPY COMBINED WITH LOWER ENDOSCOPY?**

Kody Crowell¹, Raza Patel¹, Mark Fluchel¹, Amy Lovichik², Staci Bryson², John Pohl¹, ¹Pediatric Gastroenterology, University of Utah, Salt Lake City, UT, ²Pediatric Pathology, University of Utah, Salt Lake City, UT

**BACKGROUND/AIM:** Graft-versus-host disease (GvHD) is a cause of morbidity and mortality in recipients of hematopoietic stem cell transplantation (HSCT). GvHD can include dermatologic, hepatic and gastrointestinal manifestations. The aim of this study was to assess the distribution of GvHD in gastrointestinal (GI) biopsies from the upper and lower GI tract in pediatric patients who have undergone HSCT and to determine if there was a correlation between pathologic findings and extraintestinal manifestations of GvHD.

**METHODS:** A retrospective chart review of all patients diagnosed with GvHD between 2006 and 2011 by esophagogastroduodenoscopy (EGD) or flexible sigmoidoscopy (FS) was performed. A systematic review of pathology and clinical reports was performed to determine which biopsy sites were diagnostic of GvHD and to evaluate for the possible presence of manifestations GvHD at the time of biopsy.

**RESULTS:** Nineteen patients had pathology consistent with a diagnosis of GvHD. Patients who had GvHD diagnosed by EGD also had GvHD identified by FS 100% of the time (positive predictive value (PPV) of 1). In patients that were found to have underlying liver disease, GvHD was diagnosed by endoscopy (EGD or FS) with a PPV= 0.9.

**CONCLUSION:** In this group of patients, FS was found to be equal to EGD in diagnosing GvHD. If there is a suspicion of GvHD and a patient has liver disease, GvHD likely will be diagnosed by performing FS alone. Use of FS with biopsy for diagnosis of GvHD is an effective, safe, and a less expensive diagnostic technique compared to other endoscopic interventions.

---

**GI RADIOLOGY STUDIES PERFORMED IN A PEDIATRIC COHORT OVER A NINE-YEAR PERIOD.**

Trevor Tompane¹, Ruth Bush⁴, Tanya Dansky³, Jeannie Huang¹,² ¹Pediatrics, University of California, San Diego, La Jolla, CA; ²Gastroenterology, Rady Children's Hospital, San Diego, CA; ³Childrens Physicians Medical Group, San Diego, CA; ⁴Pediatrics, Rady Children's Hospital, San Diego, CA

**Background:** Diagnostic radiology procedures (DRPs) and related ionizing radiation exposure in children are associated with increased cancer risk. Gastrointestinal symptoms are among the most common clinical complaints assessed in children, and diagnostic testing often includes DRPs. Data regarding DRPs performed in children for gastrointestinal complaints is lacking.

**Objective:** To characterize DRPs associated with gastrointestinal complaints performed in a general pediatric population cohort.

**Methods:** Radiology procedure insurance claims from 2001-2009 at an Independent Physicians Association covering a median of 61,657 patients/year and associated with a tertiary-care pediatric hospital were reviewed. Radiology procedure CPT and associated ICD-9 codes and patient demographics were retrieved from insurance claim data. Results: 11,928 DRPs were performed on 6,769 children during 2001-2009. The three most common DRPs performed for gastrointestinal complaints were plain film (59%), computed tomography (23%) and ultrasound (12%). The most common gastrointestinal-related ICD-9 codes for which DRPs were performed were abdominal pain, appendicitis, and constipation and vomiting. DRPs were most often ordered and performed in the outpatient setting (52%) with the remaining performed in the ER (30%) and inpatient (18%) settings. In our multivariate model, older children seen in the inpatient (OR=6.57) or emergency settings (OR=6.35), and imaged for appendicitis (OR=6.85), abdominal pain (OR=1.64) or abdominal mass (OR=2.12) were most likely to undergo higher radiation DRPs. CT DRPs increased by over 50% over the nine year period.

**Conclusions:** We demonstrate high clinical volumes of DRPs ordered in the outpatient setting for gastrointestinal complaints in children. Our findings may help target clinical practice interventions for reduction of radiation exposure in youth from DRPs related to gastrointestinal symptom evaluation.

Background: Carbon dioxide (CO2) insufflation during colonoscopy is routinely used in adults. A recent meta-analysis of randomized controlled trials comparing air and CO2 insufflation in adults concluded that CO2 insufflation during colonoscopy is associated with less post-procedural pain and distention without significant pCO2 variation. However, prospective pediatric studies are lacking.

Patients and Methods: A total of 100 consecutive patients undergoing outpatient colonoscopy under general anesthesia were enrolled and randomized to receive air vs. CO2 insufflation during colonoscopy. (CO2 Insufflation Device, Olympus, Center Valley, PA). Data collected included demographics, abdominal girth pre-, immediately post-procedure, and at discharge; pain assessment using patient reported 0-10 scale measurements pre-procedure and at discharge, procedure time, total recovery time, and adverse events.

Results: There were no differences in age, gender or body weight between the two groups. There were no differences between abdominal girth pre-, post-procedure and at discharge. There was no difference in procedure and recovery times. Post-procedure abdominal pain was reported by six patients in each group. There was no difference in the number of telephone calls received regarding post-procedure symptoms. No procedural adverse events were recorded.

Conclusion: Carbon dioxide insufflation appears to be safe for pediatric colonoscopy. No significant differences were detected in post-colonoscopy abdominal girth, procedure and recovery times, or pain rating comparing patients receiving air vs. CO2 insufflation. Larger pediatric studies may be necessary in order to further investigate effect of CO2 insufflation on post-procedural pain.

63 ELECTIVE LAPAROSCOPIC APPENDECTOMY FOR CHILDREN WITH CHRONIC RIGHT LOWER QUADRANT ABDOMINAL PAIN. Jose S. Lozada, Pediatric Surgery, Cleveland Clinic, Cleveland, OH. Lozada J, F Mahajan L, Seifarth

Purpose: Chronic abdominal pain or recurrent abdominal pain is common in childhood. The management of these patients stipulates responsible application of diagnostic tools without ordering unnecessary invasive investigations. Due to the high resolution rate of chronic abdominal pain, extensive testing is a subject of debate. A thorough workup should be reserved for patients with a suspected organic cause. Common etiologies range from psychosomatic disorders, intra-abdominal processes, or chronic IBD. Despite modern technology the workup remains a challenge with high potential for frustration in cases with unclear cases.

We present a series of 24 patients with chronic right lower quadrant pain. Each patient presented with a clinical picture of acute appendicitis, subsequently ruled out by imaging. All patients underwent an array of diagnostic tests before being referred to pediatric surgery.

Methods: We reviewed the medical records of 24 patients who underwent elective appendectomies for chronic right lower quadrant abdominal pain without radiographic abnormalities.

Results: There were 24 patients (9 males), ages 6-17y (mean 13.4y), duration of symptoms 1-52mo (median 16 mo). All patients underwent extensive GI workup. Patients averaged 2 colonoscopies and 2 endoscopies. Most girls underwent gynecological exams. Range of CT scans: 1-3. Cost for work-up prior to surgery averaged USD10,600 per patient. The average cost for surgery was USD4,600. Pathology was abnormal in 54% of samples. All patients reported post-operative resolution of abdominal symptoms.

Conclusion: Laparoscopic appendectomy is a valuable diagnostic and therapeutic tool. It is a quick and safe procedure with low morbidity and a short post-operative hospitalization of 5-12 hours. The pathology results suggest chronic appendicitis in the majority of patients.

Given the potentially invasive, expensive and long diagnostic trail experienced by these patients, we recommend early consideration of laparoscopic appendectomy in the care of patients with chronic right lower abdominal pain.

64 MAGNET INGESTION-RELATED EMERGENCY DEPARTMENT VISITS IN CHILDREN AND ADOLESCENTS IN THE UNITED STATES FROM 2002 TO 2010. Ali S. Khalili1,2, Chaitanya Pant3, Reinaldo Garcia1,2, Thomas J. Sferra1,2, 1UH Rainbow Babies & Children's Hospital, Cleveland, OH; 2CWRU School of Medicine, Cleveland, OH; 3University of Oklahoma HSC, Oklahoma City, OK

Introduction: The increasing availability of powerful, rare earth magnets in consumer products has been associated with recent reports of magnet ingestions leading to significant gastrointestinal complications when more than one magnet is ingested. However, the extent of this problem is unknown.

Objective: To investigate the epidemiology of magnet-related emergency department (ED) visits among pediatric patients in the United States.

Methods: We extracted pediatric cases (1 month to 18 years of age) of magnet and coin ingestions from the United States Consumer Product Safety Commission National Electronic Injury Surveillance System for the years 2002 to 2010. Cases without specific documentation of “magnet” ingestion were excluded. National historic estimates of...
ingestions were determined for 2007 to 2010 (the years for which the number of magnet ingestions was sufficient for this calculation). The Chi-square test was used to compare groups.

**Results:** We evaluated 397 cases of magnet and 10,169 coin ingestions. There was a male predominance for ingestions that approached significance (magnet, 60%; coin, 55%, P=0.059). The mean age was greater for magnet as compared to coin ingestions (4.8 vs 3.5 yrs, P<0.001). A greater proportion of magnet ingestions occurred in those ≥6 yrs of age (magnet, 34% vs coin, 18%, P<0.001). Multiple magnets were ingested in 14.6% of cases for all years with 27.5% in 2010. Magnet ingestions were more likely to be discharged home than coin (92% vs 81%, P<0.001). From 2007 to 2010 the US national estimates for magnet ingestions were between 1,329-2,025 (1,922 in 2010) and for coin 27,852-34,148 cases per yr.

**Conclusions:** Magnets pose a health hazard to children, especially those less than 5 years of age. However, older children also are at risk of accidental or intentional ingestion. All involved in the care of children must be aware of the potential risks associated with magnet ingestions.

**65 DELETERIOUS EFFECTS OF INDOMETHACIN IN THE MID-GESTATION HUMAN INTESTINE**

Corentin Babakissa¹, Perron Nancy¹, Eric Tremblay¹, Emanuela Ferretti³, Ernest G. Seidman⁴, Emile Levy¹, Daniel Ménard², Jean-François Beaulieu¹, ¹CIHR Team on the Digestive Epithelium, Department of Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada; ²CIHR Team on the Digestive Epithelium, Department of Pediatrics, Université de Sherbrooke, Sherbrooke, QC, Canada; ³CIHR Team on the Digestive Epithelium, Division of Neonatology, Department of Pediatrics, Children Hospital of Eastern Ontario, Ottawa, ON, Canada; ⁴CIHR Team on the Digestive Epithelium, Department of Gastroenterology, McGill University, Montreal, QC, Canada; ⁵CIHR Team on the Digestive Epithelium, Department of Nutrition, Centre de recherche, CHU Sainte-Justine, Montreal, QC, Canada

Background: Indomethacin (INDO) is a non-steroidal anti-inflammatory drug used for the treatment of patent ductus arteriosus in preterm infants. The use of INDO in preterm infants is associated with an increased risk of developing necrotizing enterocolitis. The goal of our study was to generate an exhaustive biological pathway analysis of the impact of INDO on the global gene expression profiles of the developing human small and large intestines at midgestation using serum-free organ cultures.

Results: We used Illumina microarrays to identify gene expression profiles in both small and large intestinal explants (ileum and colon, n=4) cultured for 48 hours in the presence of 1µM INDO. Differentially expressed genes were analyzed with Ingenuity Pathway Analysis software and revealed that INDO negatively modulated important biological functions such as "cellular growth and proliferation", "cell death", "gastrointestinal diseases", "inflammatory diseases", "immune cell trafficking", and "acute phase response signaling". More importantly, we also found that critical metabolic pathways, namely "glycolysis/gluconeogenesis", "oxidative phosphorylation" and "free radical scavenging activity", were highly repressed by INDO in both intestinal segments.

Conclusion: Our study identified that INDO exerts multiple detrimental metabolic effects on the immature human intestinal mucosa and emphasizes the need for a better understanding of the molecular mechanisms of NSAIDs in premature infants.

**66 THE ROLE OF CROHN'S DISEASE GENES IN INTESTINAL FAILURE OUTCOMES.**

Karolina M. Burghardt¹,², Vishal Avinash²,³, Christina Kosar¹, Wei Xu¹, Paul W. Wales¹,³, Yaron Avitzur¹,³, Aleixo Muise²,³, ¹GIFT Program, Hospital for Sick Children, Toronto, ON, Canada; ²Dept. Pediatrics, Hospital for Sick Children, Toronto, ON, Canada; ³University of Toronto, Toronto, ON, Canada

AIM: NOD2 polymorphisms associated with Crohn's disease were reported to be more prevalent in patients with graft failure post intestinal transplantation. We sought to determine if polymorphisms in the NOD2 signaling cascade (including NOD2) are associated with intestinal failure (IF) or its complications. METHOD: We carried out a cross-sectional study of 59 children with IF and 1000 healthy Caucasian adult controls. Using the Taqman platform we determined the prevalence of NOD2 SNPs (rs2066844, rs2066845, rs2066847) as well as of ATG16L1 (rs2241880), RAC1 (rs10951982), and CARD9 (rs4077515). NOD2 pathway polymorphisms were evaluated in relation to sepsis, ICU admissions, liver failure and need for transplant. RESULTS: Most patients were born prematurely (n=38, 65%) having an anterior wall defect (n=14, 24%), intestinal atresia (n=13, 22%) or NEC (n=12, 20%). Over half of the patients had > 2 episodes of sepsis in the first year of TPN use (n=30) and 20% (n=12) had >1 episode of fungal sepsis. Half of the patients (n=29) required TPN for > 1 year. Severe liver failure (conjugated hyperbilirubinemia > 100 micromol/L) developed in 25% of patients (n=15). Transplant assessment was initiated in 20% (n=12) and 6 patients received a liver and/or small bowel transplant. There were no differences between cases and controls in the prevalence of the NOD2 SNPs nor their related signaling molecules. Minor allele of CARD9 was associated with decreased Odds of sustained conjugated hyperbilirubinemia (p=0.036; OR 0.25). Patients having the minor allele of ATG16L1 tended to have decreased Odds of > 2 episodes of sepsis (p=0.054, OR 0.48).

CONCLUSIONS: Patients with the minor allele of CARD9 were less likely to have progressive liver disease, and those with ATG16L1 tended to have decreased Odds of sepsis. Genetic alterations in host innate immunity are associated with susceptibility to progressive IF associated liver disease and septic episodes in patients with IF.
67 POSITIVE TISSUE TRANSGLUTAMINASE ANTIBODY TITERS (TTG-IGA) WITH NORMAL HISTOLOGY: THE DIFFERENCE BETWEEN AT RISK AND SYMPTOMATIC GROUPS.
Osama F. Almadhoun1, Philip Katzman2, Thomas Rossi1,1 Pediatric, University of Kansas Medical Ctr, Kansas City, KS; 2University of Rochester Medical Center, Rochester, NY

Objectives: The aims of this study were to assess the significance of positive tTG titers and normal duodenal histology in patients with conditions known to be at risk for Celiac Disease (CD) compared with symptomatic children and to evaluate the influence of diet on tTG titers in each group and its relation to symptoms in the symptomatic group.

Patients and Methods: All patients with positive tTG titers and normal histology during a 60-month period were included. Patients with known biopsy proven CD were excluded. Indications for testing were either being at risk for CD (group 1) or symptoms suggestive of CD (group 2). Additional data analyzed also included HLA typing, EMA antibodies, in addition to demographics, and repetitive tTG measurements for follow-up.

Results: A total of 300 charts of patients with positive tTG's were reviewed. 74 patients with normal histology were included in the study, 27 belonged to group 1 and 47 to group 2. There was no difference in the mean tTG titers between the two groups. The degree of seropositivity and histological changes were also similar. Patients belonged to at risk group were more likely to have their tTG titers improve spontaneously and less likely to have it improve on gluten free diet. Symptomatic patients had better response to gluten free diet.

Conclusion: Symptomatic Children with positive celiac serology and normal histology may benefit from gluten free diet. The benefit of Gluten free diet in at-risk patients is unclear. Endomysial antibodies and HLA typing in this group may help to determine the degree of suspicion for future development of celiac disease.

68 FACILITATING RECRUITMENT THROUGH DEVELOPMENT OF A RESEARCH REGISTRY
Elaine Leonard Puppa, Alessio Fasano, Center for Celiac Research, University of Maryland, Baltimore, MD

In the United States, HIPAA privacy regulations require permission from potential subjects for research. Establishment of a research registry can facilitate screening for potential research subjects by creating a list of persons who have expressed interest and agreed to be contacted for research. Over 300 new patients are scheduled at the Center for Celiac Research clinic each year. The clinic occurs 3 times a month. At the beginning of each new patient visit the research nurse introduces herself, and explains that all patients attending clinic are asked if they would like to participate in the research registry. If the patient expresses interest, the IRB approved consent and HIPAA form are reviewed and the patient is given an opportunity to ask questions. The patient is given an opportunity to discuss it with any family present and adequate time for consideration. At the end of the clinic visit the research nurse asks if the patient has any further questions or would like to participate. If the patient agrees the informed consent and HIPAA release are signed and a copy is given to the patient. A copy of the signed consent is placed in the patient's medical chart and the original is filed with the research registry documents. After consent is signed, the coordinator reviews the medical chart for eligibility for any currently recruiting studies. The patient's name is entered into a research data base with the date of consent and demographic information. In a roughly 3 year period over 800 patients were recruited to participate in the registry. 98% of patients approached for permission to use records gave consent. 99% of the consented gave permission to be contacted regarding future research. Of the patients consenting to participate in the registry, 136 participated in additional trials. Conclusions: Use of the research registry has enhanced recruitment for other research studies and facilitates the chart review for retrospectives studies. It avoids the need for a HIPAA waiver and reduces review time. Because of the high participation, the data accurately reflects practice demographics.

69 CALCIUM-SENSING RECEPTOR INHIBITS CHOLERA TOXIN-INDUCED ANION SECRETION BY INTESTINE VIA ENTERIC NERVOUS SYSTEM. Catherine Y. Cheng1, Ekaterina Petrova1, Max Stahl1, Sam Cheng1,2,1 Yale University, New Haven, CT; 2University of Florida, Gainesville, FL

Cholera toxin induces diarrhea by direct epithelial cell generation of cyclic nucleotide as well as stimulation of enteric nervous system (ENS) to release secretagogues. We have previously demonstrated that calcium-sensing receptor (CaSR) agonists can abrogate cholera toxin-stimulated fluid secretion in ENS-absent colonic epithelial crypts by increasing phosphodiesterase-dependent cyclic nucleotide degradation. Given that CaSR is expressed in tetradotoxin (TTX)-sensitive neurons comprising ENS, we hypothesized that CaSR agonists may also function through modulation of neuronal pathways. To examine this, rat colon segments containing intact or partial ENS were isolated and mounted onto Ussing chambers, and TTX-sensitive short-circuit current (Isc) responses to serosally applied CaSR agonist R-568 were examined. Consistent with active regulation of anion secretion by ENS, a large proportion of Isc in the proximal and distal colon was TTX-sensitive, both at basal and cholera toxin-stimulated conditions. This TTX-sensitive neurally mediated Isc was significantly inhibited upon activation of CaSR with R-568. A similar inhibitory effect of R568 was observed following neural stimulation with neurotransmission activator veratridine. The antisecretory effect of R568 appears to be mediated primarily by submucosal plexus because removal of muscular layers and myenteric plexus from colon did not significantly reduce inhibitory effect.
of R568. Atropine-sensitive cholinergic and VIPergic neurons in the submucosal plexus are known to actively regulate anion secretion. The inability of atropine to abolish the R-568 effect suggests that CaSR-mediated ENS inhibition is mostly exerted via VIPergic and less through cholinergic neurons. Our results suggest a new model in which neuronal component of intestinal fluid transport can be modulated by inhibitory effects of CaSR on ENS. The ability of CaSR agonist to reduce cholera toxin-stimulated anion secretion suggests that modulation of CaSR activity may provide a new therapeutic approach to cholera and other secretory diarrheas.

**70 EFFECTS OF 70% ETHANOL LOCKS ON RATE OF CENTRAL LINE INFECTION, THROMBOSIS, BREAKAGE, AND REPLACEMENT IN A COHORT OF PEDIATRIC PATIENTS WITH INTESTINAL FAILURE.** Maisam Abu-El-Haija, Riad Rahhal, University of Iowa, Iowa City, IA

Background: Parenteral nutrition is essential for the growth and nutrition of patients with intestinal failure (IF). Catheter related bloodstream infections (CRBSI) are a major complication of parenteral nutrition use. Preventing CRBSI is essential to the management of IF patients, since sepsis is associated with loss of central line access, liver disease and death. Few retrospective studies have shown that 70% Ethanol lock therapy (ETL) for central lines can reduce the infection rate. Studies that look at central line breakage, thrombosis and replacement with the use of ETL are lacking. Methods: This is a retrospective chart review, the primary outcome was the CRBSI rate per 1,000 catheter days, and the secondary outcomes were line thrombosis, line breakage, and line replacement rates with use of ETL compared to heparin locks. This study was approved by the institutional review board. Results: We identified 12 patients with intestinal failure who are TPN dependent over the course of the study period. 10 patients satisfied the inclusion criteria and were included in the analysis. Mean age at enrollment was 37 months of age, 80% were females, and total number of days on heparin locks and ETL were 2655 and 3082 days respectively. Number of infections decreased from 8.67 on heparin lock therapy to 3.24/1,000 catheter days on ETL. Line thrombosis increased from 0.38 to 2.9/1,000 catheter days on ETL. Line repair increased from 0 to 6.8/1,000 catheter days on ETL. Line replacement rate due to infection decreased (from 3.01 to 0.65/1000 catheter days) while line replacement rate due to line thrombosis or breakage increased (from 0 to 1.30/1000 catheter days) on ETL. Conclusion: ETL therapy is an effective method for decreasing CRBSI, however it can have a negative impact on line integrity. Patients should be carefully selected when deciding on ethanol lock use for central line care. Studies are needed on the effect of different ethanol concentrations on infection rate as well as line integrity to optimize the outcome in this population.

**71 GASTROINTESTINAL INFLAMMATION AND INTESTINAL PERMEABILITY IN CHILDREN WITH AUTISM SPECTRUM DISORDER.** Timothy Buie¹, R. Kushak¹, K. Murray¹, C. Chen¹, E. Nestoridi¹, D. Newburg², H. Winter¹, ¹Pediatrics, MassGeneral Hospital for Children, Boston, MA; ²Boston College, Boston, MA

Gastrointestinal problems in children with autism spectrum disorders (ASD) are thought to be common, but the mechanisms are not known. Previous studies suggest that increased intestinal permeability may contribute to intestinal dysfunction. We report a series of 111 children--61 with ASD, 50 without ASD -- who were enrolled at the time of clinically indicated diagnostic endoscopy and ileo-colonoscopy to have an intestinal permeability study with rhamnose and lactulose. Stool was collected to evaluate fecal lactoferrin and calprotectin proximate to the procedure.

Methods: Following intubation of the duodenum, the solution of rhamnose and lactulose was infused into the duodenum. Urine was collected for five hours following the administration of the solution. Biopsies of the various regions of the GI tract were obtained for histology. The clinically indicated duodenal biopsies were snap frozen for analysis of disaccharidase activity.

Results: By histology, 7 (11%) had esophagitis, 6 (10%) had gastritis, 4 (7%) had duodenitis, 3 (5%) had ileal inflammation and 12 (19%) had colonic inflammation. The patients with ileal or colonic inflammation had mild and non-specific changes and none of the subjects with duodenitis had serologic or histologic evidence of celiac disease. In children with ASD, 28/61 had some intestinal inflammation, and of those, 4 had duodenal inflammation. No differences in rhamnose/lactulose ratios (study permeability markers) between non-inflamed controls and non-inflamed/inflamed ASD subjects were demonstrated using the Wilcoxon Rank test. Stool calprotectin and lactoferrin studies do not appear to predict which patients with ASD have intestinal inflammation.

Conclusions: Children with autism and gastrointestinal symptoms prompting endoscopic evaluation may have non-specific inflammatory changes. Non-invasive biomarkers including intestinal permeability studies, fecal calprotectin and lactoferrin levels may not predict which children will have significant gastrointestinal inflammation or pathology.
72 A PROSPECTIVE STUDY OF THE PREVALENCE OF ENDOSCOPY-RELATED COMPLICATIONS IN CHILDREN. Robert E. Kramer, Digestive Health Institute, University of Colorado/Children's Hospital Colorado, Aurora, CO

Background: The few prospective studies on endoscopic complications in children focus on identified outcomes such as perforation or bleeding without including symptomatic complaints that may result in unanticipated evaluation and costs.

Objective: To determine the prevalence of post-procedural complications in pediatric patients undergoing endoscopy at a large, tertiary-care, academic institution.

Methods: All reported complaints, emergency department visits and hospital admissions within 72 hours of an endoscopic procedure were prospectively tracked over a two year period (July 2010 - June 2012), using data from parent phone calls, fellow documentation and specific queries of the EMR.

Results: A total of 4102 endoscopic procedures were performed over the 24 month period of study, including 3028 EGD’s, 824 colonoscopies, 162 sigmoidoscopies, 44 ERCP’s and 35 enteroscopies. There were a total of 99 complications, resulting in a complication prevalence of 2.41%. Sixty-nine of these complications (1.68%) were moderate or severe, defined as requiring ED evaluation, hospital admission, blood transfusion, surgery or other significant morbidity or mortality. Of these, 49 (1.19%) were ED evaluations alone and 20 (0.49%) required hospital admission. Complications were divided into categories including abdominal pain (29%), fever (23%), bleeding (14%), chest pain (8%), respiratory/anesthesia (7%), throat pain (5%), perforation (3%), vomiting (4%), pancreatitis (3%), technical (2%) and other (2%). Complication prevalence for procedures performed by fellows was 2.58% versus 2.31% for Attendings (p=0.6). The risk associated with interventional procedures was greater than for diagnostic ones (OR 2.75, p=0.0002). The average charges accrued for an ED evaluation in these patients was $3500.

Conclusions: Though the prevalence of actual perforation, infection or blood transfusion was low, symptoms significant enough to warrant ED referral and/or admission may be higher than anticipated and represent significant morbidity and costs associated with endoscopic procedures in children.

73 MEASURING COLONOSCOPY QUALITY IN PEDIATRICS - A QUALITY IMPROVEMENT INITIATIVE. Esther J. Israel1, Kristen Solemina1, Evanthia Kartsagoulis2,1Pediatrics, Massachusetts General Hospital, Boston, MA; 2Performance Analysis and Improvement, Massachusetts General Hospital, Boston, MA

Quality measures for pediatric colonoscopy have not been delineated. The goal of this project was to create a quality improvement program around potential quality measures for colonoscopy in pediatric patients. METHODS: The documentation of 3 components, modified from the adult criteria for a quality colonoscopy, were evaluated: 1. Pre-procedure risk assessment -ASA grade, history and physical done with allergies reviewed, and patient/procedure ID and verification; 2. Quality of the bowel prep; and 3. Success of reaching the ileum. A composite measure of these 3 components was considered indicative of a quality colonoscopy. All colonoscopies performed by the pediatric endoscopists at our institution were included. Procedures documented as being "aborted" or "difficult" were excluded. A report of performance for each individual MD and a blinded report of the group's performance, was reported to the physician monthly in 2011. RESULTS: Colonoscopies performed by 18 practitioners in 2011 were evaluated. There was a range per physician of 5-101 eligible colonoscopies. Composite measure rates of 58% and 51% were noted in 2009 and 2010, respectively. The rate increased to 81% in 2011. Of the individual measures, the documentation of prep quality was most improved from 67% to 92%. An increase from 81% to 90% was noted in the ileum being reached. Additionally, the post-intervention range for the individual endoscopists was 60 to 100% for ileal intubation, with 10/18 reaching the ileum >90% of the time. CONCLUSIONS: 1. With continuous monitoring of quality parameters, the quality of colonoscopy reporting and performance can be improved. 2. The mean ileal intubation measure of 90% is the first report of such a measure. As the most common indications for colonoscopy in children are abdominal pain and diarrhea, ileal biopsy is often important. These type of data are necessary for the practice evaluation of pediatric endoscopists and might be considered in setting training goals.

74 CAN PEDIATRIC GI FELLOWS MEET THE CURRENT NASPGHAN PROCEDURAL COMPETENCY GUIDELINES? Diana G. Lerner1, Bhaskar Gurram1, Khalil El-Chammas1, Yi Goh1, Linda Anderson2, Petar Mamula2, Praveen Goday1, B. Li1, Bernadette Vitola1, 1Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Special Procedures, Children's Hospital of Wisconsin, Milwaukee, WI; 3Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA

In 1999 NASPGHAN defined the number of specialized GI procedures required to achieve competency during a 3-year pediatric GI fellowship. Unlike adult GI programs, discordance between current training guidelines and actual experiences by pediatric GI fellows has been reported by two surveys. The aim of this study was to assess the maximal number of opportunities for therapeutic endoscopy and liver biopsies afforded to pediatric GI fellows during a 3-year period.

Methods: Data were collected from 7 US pediatric GI fellowship programs via CPT codes and endoscopy database
query for procedures completed between 2009-2011. Participating centers completed a questionnaire about ancillary opportunities for endoscopic training.

Results: Few programs meet the NASPGHAN 1999 procedural guidelines (Table 1). Control of non-variceal bleeding and polypectomies were uncommon in all pediatric institutions. PEG placement opportunities were sufficient at most centers in which pediatric GI participates in the procedure. Ancillary procedural training including simulator experience, hands on courses and/or adult GI rotation are offered by 71% of programs.

Discussion: Attaining the recommended numbers of specialized procedures required to meet competency standards may be difficult. Exposure to specialized GI procedures is uncommon and varies widely in pediatric GI training programs independent of size. There is a need for alternative modalities for training such as hands-on endoscopy courses, simulations, and adult endoscopy rotation, which are currently offered by most programs. Future guidelines may need to reflect limitations in training.

### Comparison of NASPGHAN Procedural Competence Guidelines versus Maximal Opportunities Afforded to Fellows in a 3-year Period

<table>
<thead>
<tr>
<th>Procedure</th>
<th>NASPGHAN Competency Requirement</th>
<th>Range of Maximum # of Procedures per Fellow</th>
<th>Percent of Programs Meeting Competency Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal, pyloric and duodenal stricture dilation</td>
<td>20</td>
<td>0-53</td>
<td>28%</td>
</tr>
<tr>
<td>Foreign body removal</td>
<td>5</td>
<td>3-22</td>
<td>71%</td>
</tr>
<tr>
<td>Percutaneous endoscopic gastrostomy placement</td>
<td>10</td>
<td>0-80</td>
<td>50%</td>
</tr>
<tr>
<td>Percutaneous liver biopsy</td>
<td>20</td>
<td>12-33</td>
<td>57%</td>
</tr>
<tr>
<td>Control of non-variceal bleeding</td>
<td>20</td>
<td>0-5</td>
<td>0%</td>
</tr>
<tr>
<td>Polypectomy</td>
<td>20</td>
<td>1-19</td>
<td>0%</td>
</tr>
<tr>
<td>Sclerotherapy/Band Ligation</td>
<td>15</td>
<td>0-16</td>
<td>28%</td>
</tr>
</tbody>
</table>

---

75 PEDIATRIC GASTROENTEROLOGY PRACTICE PATTERNS AND SATISFACTION: RESULTS OF A SURVEY. Claire Wilson1, Linda Muir2, 1Providence Alaska Medical Center, Anchorage, AK; 2Oregon Health Sciences University, Portland, OR

1729 members of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition were electronically asked to participate from 12/06/2011-04/30/2012 in a 52-question survey regarding practice patterns, demographics and career satisfaction. 565 (33%) members began the survey and 507 (29%) completed it. Respondents had the option to skip questions. The most common practice situation was academic primarily performing clinical duties, followed by clinical work as employee of a hospital or HMO. General pediatric gastroenterology was practiced by 89%, 9% practiced mostly in the area of hepatology/transplant, and 2% practiced primarily nutrition. 64% of respondents were male. The most common age bracket was 50-55 years (21%) followed by 36-39 years (17%). The majority of solo practitioners were 50-59 years of age and the majority of those doing primarily research were 36-45 years of age. 66% of respondents were Caucasian, 10% South Asian, 9% Hispanic or Latino, 9% Asian, and 2% African-American. 45% had been at their current institution for 0-5 years. 40% worked 41-50 non-call hours per week, and 31% worked 51-60 hours. 44% worked at 2 or more locations 10 or more miles apart each week, tending to be those in private practice. 16% needed a translator for 21% or more of their patients. An equal percent of respondents (43% for each) reported performing 0-5, and 6-10 procedures per week. The most common base yearly salary bracket (for 36%) was $150,001-200,000; 63% were in the $150,001-250,000 range. 68% were satisfied or very satisfied with the way their career had turned out or was evolving; 21% were neutral. Most felt it had been moderately easy to achieve adequate equipment, space, nursing and clerical staff; most found it difficult to balance work and family, and to negotiate financial issues. Location was most often cited (by 81%) as important in choosing a practice setting, followed by opportunity for desired career experience (52%), academic affiliation (49%), reputation of group (48%), and group size (45%).
76 GENDER FACTORS AMONG PEDIATRIC GASTROENTEROLOGISTS. Claire Wilson1, Linda Muir2, 1Pediatric Gastroenterology, Providence Alaska Medical Center, Anchorage, AK; 2Oregon Health Sciences University, Portland, OR

There have been reports of gender disparity among adult gastroenterologists. To see whether this was also apparent in pediatric gastroenterology despite the longstanding preponderance of women in pediatrics, 1729 members of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition were electronically invited to participate from 12/06/2011-04/30/2012 in a 52-question survey regarding practice patterns, demographics and career satisfaction. 565 (33%) members began and 507 (29%) completed the survey, with the option to skip questions. 468 responded to the question identifying gender; 64% were men. Higher age brackets tended to have higher percentages of men. 19% of women and 9% of men had no children. 70% of men and 61% of women were Caucasian, 10%/12% South Asian, 8%/11% Hispanic or Latino, 6%/13% Asian, and 2%/1% African-American. The most common work situation (for 46% of men, 54% of women) was academic primarily performing clinical activities. In traditional tenure tracks 44% of men and 9% of women were full professors; in clinician-educator tracks 29% of men and 10% of women were full professors. 36% of men and 47% of women worked 41-50 non-call hr/wk; 47% of men and 36% women worked > 50 hr/wk. The most common range (27% of men and 35% of women) of inpatient + outpatient visits/wk was 31-45; 19%/25% did 16-30 visits per week and 25%/17% did 46-60 visits per week. 38% of men and 50% of women did 0-5 procedures/wk, 44%/41% did 6-10, 12%/6% did 11-15, and 3%/2% did 16-20. Lower brackets for base yearly compensation were more often associated with female gender. Division Chair, Fellowship Director and Chair of a Department Committee were more likely to be men. Although larger numbers of men in the higher age brackets may have confounded gender comparisons of professional status and salary, of those 56-59 years of age and working full time, men reported higher base salaries than women. 74% of men and 58% of women were very satisfied or satisfied with how their careers were evolving. 3% of men and 34% of women believed gender had affected their career advancement.

Hepatobiliary/Transplant

92 A NOMOGRAM PREDICTING THE RISK OF NON-ALCOHOLIC STEATOHEPATITIS IN PEDIATRIC PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE. Katharine Eng1, Nishaben Patel1, Katherine Melville2, Rocio Lopez3, Valerio Nobili3, Naim Alkhouri1,2, 1Department of Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH; 2Digestive Disease Institute, Cleveland Clinic Foundation, Cleveland, OH; 3Bambino Gesu Children's Hospital, Rome, Italy

Introduction: Nonalcoholic fatty liver disease (NAFLD) affects 10% of children in the United States. Its most severe form, nonalcoholic steatohepatitis (NASH), is associated with increased liver-related morbidity and the development of cirrhosis in childhood. Currently the differentiation between simple steatosis and NASH remains a histologically driven diagnosis. Here we aimed to develop a non-invasive predictive model of NASH in pediatric patients with NAFLD. Methods: Utilizing a cohort of pediatric patients with NAFLD, multivariable logistic regression analysis was employed to create a nomogram predicting the risk of NASH on liver biopsy. An automated stepwise variable selection method was used to choose the final model. Internal validation of the model was performed by means of bootstrapping, and calibration was assessed graphically. Results: Our cohort consisted of 302 patients with a mean age of 12.3 ± 3.1 years, a mean BMI percentile of 94.3 ± 6.9, and the presence of metabolic syndrome in 55.6% of the cohort. NASH was present in 67% of the patients. Following stepwise variable selection, the presence of metabolic syndrome, triglyceride levels, waist circumference percentile, and total bilirubin were included as predictive variables in the model. The nomogram demonstrated good discrimination with an area under the receiver operating characteristics curve of 0.742. The model calibration was also noted to have good agreement between observed and predicted probabilities. Conclusions: We constructed a nomogram that predicts the risk of NASH in pediatric patients with NAFLD with reasonable accuracy. If validated externally, this tool could be utilized as a non-invasive method to diagnose NASH in children.

93 NON-HIGH-DENSITY LIPOPROTEIN CHOLESTEROL (NON-HDL-C) LEVELS IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD). Katharine Eng1, Nishaben Patel1, Katherine Melville2, Rocio Lopez3, Valerio Nobili3, Naim Alkhouri1, 1Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH; 2Digestive Disease Institute, Cleveland Clinic Foundation, Cleveland, OH; 3Bambino Gesu Children's Hospital, Rome, Italy

Introduction: NAFLD is associated with increased cardiovascular disease (CVD) risk in children, with an even further increase in patients with nonalcoholic steatohepatitis (NASH). Non-HDL-C has been shown to be a good predictor of cardiovascular events. Recent data in adults found NASH to be associated with significantly higher levels of non-HDL-C than simple steatosis, suggestive that it might be useful as a non-invasive tool to diagnose NASH. The goal of our study was to assess non-HDL-C levels in children with NAFLD. Methods: Patients with biopsy-proven NAFLD were included in the analysis. Univariable analysis was performed to assess differences in demographic and clinical characteristics between subjects with and without NASH. Spearman rank correlation coefficients were calculated to assess the correlation between non-HDL-C levels and clinical variables. Results:
Data was collected from 302 patients with NAFLD; 203 with NASH and 99 without NASH. Patients with NASH had higher waist circumference percentile, triglyceride levels, AST, GGT, and higher prevalence of metabolic syndrome than those with simple steatosis (p < 0.05). Subjects with NASH were found to have significantly higher non-HDL-C levels than those without NASH (105.8 ± 40.2 vs 92.3 ± 32.8; p = 0.004). However, after adjusting for the presence of metabolic syndrome, the association between non-HDL-C and NASH was not significant (adjusted mean [95% CI]: 102 [97.4, 106.6] vs 100.1 [93.4, 106.9]; p = 0.66). Additionally, histologic features were not found to be strongly correlated with non-HDL-C levels. Conclusions: Non-HDL-C levels are higher in children with NASH than those with simple steatosis, suggesting increased CVD risk. However, this may be a reflection of the higher prevalence of metabolic syndrome. Non-HDL-C had a weak association with histologic features of NASH. Thus, our results call into question the utility of non-HDL-C as a sole potential biomarker for NASH in children.

94 RELATED LIVING DONOR LIVER TRANSPLANTATION IN CHILDREN: A SINGLE-CENTER EXPERIENCE FROM LATIN AMERICA. Victoria P. Fernandez de cuevas, Gustavo Boldrini, Camila Sanchez, Daniel D Agostino, Division of Pediatric Gastroenterology and Hepatology, Liver and Intestinal Transplant Center. Pediatric Department, Hospital Italiano, Buenos Aires, Argentina

Introduction: Living related donor (LRD) increases the supply of organs for liver transplantation (LTx), decreasing waiting list mortality. In Argentina the first LTx with LRD was performed in April 1992 at the Italian Hospital of Buenos Aires.

Objectives: To evaluate and analyze the first 100 patients transplanted with LRD in a single center in Latin America. Compare differences variables as age, weight, actuarial survival and length of hospitalization between transplanted with LRD with left lateral segment and those who needed mono segment (hiper-reduction technique).

Methods: A retrospective and descriptive study of our population was done. 308 patients went through liver transplantation in our Center between 1992-2011, 100 of them (32%) were performed with LRD.

Results: 63 women and 27 males. The median patient age at transplant was 1 year and 11 months (range 0.5 -14 years) and median body weight was 9.9 kg (range 6 - 40). Biliary atresia was the most common etiology (76%). The acute rejection rate was of 51% and 40% presented biliary complications.

34 children required no segment by hyper-reduction as an alternative surgical technique. The median age of this population was 11.5 months (range 6-15) with a median body weight of 7.9 kg (range 6-10).

The actuarial survival rate at one year was 92% and 83% after 5 years for the entire population. The hyperreduced group showed a survival rate of 93% at one year.

The mean total length of hospitalization was 35 days (SD 16) in the hyperreduced group and 31 days (SD18,2) in those were transplanted with left lateral segment; there were not significant differences (p: 0.339) between these groups.

Seven patients required retransplantation.

Conclusions: Living donor transplantation represents a valuable treatment option when the supply of organs is poor. New techniques allow transplant to children with low weight and age with good results in our experience.

95 UTILITY OF PROCALCITONIN IN DETERMINING INFECTION IN PEDIATRIC LIVER-SMALL BOWEL TRANSPLANT AND INTESTINAL REHABILITATION PATIENTS. Richard Lirio, Anna Trauernicht, Robert Chaplin, David Mercer, Wendy Grant, Ruben E. Quiros-Tejeira University of Nebraska Medical Center, Omaha, NE

Background: Procalcitonin (PCT) has been shown to be an effective biomarker for bacterial sepsis. However, its effectiveness has yet to be proven in Pediatric Liver-Small Bowel Transplant (PL-SBtx) and Intestinal Rehabilitation Program (IRP) patients. In other patient populations, it has been utilized to determine time of initiation and duration of antibiotics (Abx). Some research also suggests possible use of PCT in differentiating infections from rejection.

Methods: A retrospective chart review was done on 11 patients in the PL-SBtx and IRP Programs at the University of Nebraska Medical Center from October 2011 to April 2012. PCT values were compared to each patient's work-up to assess for correlating infection. Based on the laboratory's interpretation, in patients with suspected lower respiratory tract infections (LRTI), Abx were encouraged in PCT > 0.25 ng/ml. In patients with suspected sepsis and PCT > 0.5 ng/ml, Abx were encouraged, while for levels > 2.0 ng/ml, Abx were strongly encouraged.

Results: 26 PCT levels were drawn over the 6 month span. 7 patients were post-transplant and 4 were IRP patients with short bowel syndrome. In the post-transplant patients, LRTI was suspected in 4 of the 7 patients, all with corresponding elevated PCTs. Higher PCT levels were noted in viral infections with concurrent bacterial infections. In the 3 post-transplant patients with suspected sepsis, PCT levels correlated well with the initial diagnosis of infection and decreased as treatment progressed. In the IRP patients, 3 of 4 presented with central line sepsis and their PCT levels also correlated well - one patient's initial PCT of 14.23 decreased 3 days later to 0.73 with removal of the infected line. Rejection was ruled out in all patients.

Discussion: Elevated PCT levels correlated well with infection. PCT levels trended downward as therapy was initiated or infected central lines were removed. PCT could serve as a useful marker in managing antibiotics for PL-SBtx and IRP patients.
96  MULTIPLE MODELS OF NONALCOHOLIC STEATOHEPATITIS IN ZEBRAFISH UNDERSCORE THE IMPORTANCE OF METABOLIC AND INFLAMMATORY PATHWAYS IN DISEASE PATHOGENESIS. Randolph P. Matthews1,2, Steven F. EauClaire1, Shuang Cui1, Angela Edens1
1Division of GI, Hepatology, and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; 2Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Pediatric nonalcoholic steatohepatitis (NASH) is becoming an increasingly prevalent disease, and is now the most common cause of chronic liver disease in children. One of the most pressing issues in caring for children with NASH is a lack of effective therapy other than weight loss. Zebrafish are an ideal model for drug screening, as they are highly amenable to high throughput studies such as small molecule screens. We have developed several zebrafish models of NASH, including genetic (ahcy−/−), chemical (valinomycin, deazaadenosine), and now a nutritional model elicited by exposing larval zebrafish to fructose. Increased consumption of fructose has been linked to the increased incidence of obesity in developed countries and in the pathogenesis of NASH. When compared to glucose-treated controls, both fructose- and sucrose-exposed zebrafish larvae develop steatosis. Fructose-treated larvae demonstrate mitochondrial abnormalities, as we have reported previously for both ahcy mutants and deazaadenosine-treated larvae. Our models are associated with increased inflammatory gene activity and oxidative stress, and we have reversed the steatosis in several of our models by treating with morpholino antisense oligonucleotides targeting TNFα. Our studies demonstrate that zebrafish are an excellent model organism to study NASH, and that future small molecule screens to uncover potential therapeutic agents may yield promising treatments for NASH.

97  THE ROLE OF AMP ACTIVATED PROTEIN KINASE IN PEDIATRIC NON ALCOHOLIC STEATOHEPATITIS (NASH). Zebunnissa Memon1, Susan S. Baker1, Ji Li1, Wensheng Liu1, Robert D. Baker1, Lixin Zhu1, 1Digestive Diseases and Nutrition, University of Buffalo, Buffalo, NY; 2Department of Pharmacology and Toxicology School of Medicine and Biomedical Sciences, University of Buffalo, Buffalo, NY

Introduction: An increasing number of children are diagnosed with non-alcoholic steatohepatitis (NASH). Metformin has been used in clinical trials for treating NASH but results are inconclusive. Metformin acts by activating AMPK, a protein responsible for regulating carbohydrate and lipid metabolism. It consists of 3 subunits: alpha (α) with isoforms 1 and 2, beta (β) with isoforms 1 and 2 and gamma (γ) with isoforms 1, 2 and 3. It is activated by phosphorylation on its alpha subunit. The aim of this study is to test the hypothesis that AMPK expression and/or activity is altered in NASH. Methods: NASH was diagnosed according to Kleiner's criteria. The mRNA levels of AMPK subunits in liver tissue of NASH and normal control (NC) were examined by microarray and quantitative real time PCR. Western blots were performed to examine the protein levels of AMPK subunits, total alpha AMPK and phosphorylated AMPK (active form) in NASH and NC. Results: Quantitative real time PCR results indicated that the mRNA of all AMPK isoforms was increased in NASH versus NC. The most profound increase was found with Alpha 1 (7.11 fold versus NC; p<0.05) and β1 (6.81 fold versus NC; p<0.05). However, the protein levels of total alpha and phosphorylated AMPK were decreased in NASH. In addition, there was a negative correlation between the grade of steatosis and phosphorylated AMPK protein expression. Discussion: AMPK level in human NASH livers was decreased compared to controls. AMPK activity is reduced in NASH liver compared to NC; this would explain why Metformin would not induce hepatic AMPK in human NASH livers. Increased AMPK mRNA expression in NASH livers seems to be a compensatory response to the decreased AMPK level. LKB1 is a master kinase that was recently found upstream of the AMPK pathway. It is involved in phosphorylation of AMPK. We are testing the hypothesis that the decreased AMPK activity in NASH liver is mediated by decreased LKB1 level in NASH livers.

98  HEPATITIS A AND HEPATITIS B VIRUS IMMUNITY IN PEDIATRIC PATIENTS WITH FATTY LIVER: A PILOT STUDY. Jonathan Moses1, Angela Shannon1, Suraj Thangada1, Rocio Lopez2, Naim Alkhouri1, 1Pediatric Gastroenterology, The Cleveland Clinic, Cleveland, OH; 2Quantitative Health Sciences, The Cleveland Clinic, Cleveland, OH

Vaccines for hepatitis A virus (HAV) and hepatitis B virus (HBV) are part of the routine immunization schedule in the United States. Patients with fatty liver disease are potentially at increased risk of severe liver disease if infected with either HAV or HBV. The primary aim of our study was to assess the rates of HAV and HBV immunity in a population of pediatric patients with fatty liver. Methods: We screened 27 consecutive patients in our Pediatric Preventative Cardiology and Metabolic Clinic seen between 2011 and 2012. The patients were categorized as being overweight or obese based on body mass index (BMI) percentile. The diagnosis of fatty liver was established by liver ultrasonography (US). HBV immunity was assessed by qualitative anti-hepatitis B surface antibody testing and HAV immunity was assessed by qualitative anti-hepatitis A antibody testing. Patient demographics were collected along with anthropometrics, laboratory data and liver US results. Results: The mean age of the overall cohort was 13.6 ± 3.2 years, with 77.8% male and 74% of Caucasian ethnicity. 63% of patients were characterized as obese and 23% of patients were characterized as overweight. The rate of HAV immunity was 18% and the rate of HBV
immunity was 71%. The patients without HBV immunity were more likely to have a past history of asthma and have a higher waist circumference (p = 0.038 and p = 0.019). There was no significant age difference between either group. **Conclusion:** In this pilot study, we found a large number of patients with fatty liver to be non-immune to HAV and a significant minority of patients non-immune to HBV. Age did not play a role in non-immunity for either HAV or HBV. Patients with immunity to HBV tended to have a history of asthma and higher waist circumference. This pilot data suggests more research should be performed to better assess the rate of HAV and HBV immunity and the need for booster or full series immunizations in these patients at risk for severe liver disease.

**99 CORRELATION OF IRON RELATED GENES AND OXIDATIVE STRESS IN NON-ALCOHOLIC STEATOHEPATITIS.** Diana A. Moya1, Susan S. Baker1, Wensheng Liu1, Michael D. Garrick2, Robert D. Baker4, Lixin Zhu1, 1Pediatrics Gastroenterology, University at Buffalo, Women and Children's Hospital, Buffalo, NY; 2Department of Biochemistry, University at Buffalo, Buffalo, NY

**Purpose:** Non-Alcoholic Fatty Liver disease (NAFLD) is characterized by macrovesicular steatosis. The histologic spectrum of this disease ranges from simple steatosis to non-alcoholic steatohepatitis (NASH). Oxidative stress is involved in the pathogenesis of NASH. Iron may also play a role since it is involved in reactive oxygen species metabolism. Studies have shown abnormal iron indices and elevated hepatic iron concentration in NASH. We hypothesized that increased oxidative stress in NASH livers leads to increased expression of catalase and iron related genes.

**Methods:** Data from pediatric patients undergoing a liver biopsy for suspected NASH was included. Serum iron indices, total iron, ferritin, total iron binding capacity, transferrin saturation and soluble transferrin receptor from NASH patients were compared to normal controls (NC). We analyzed gene expression of transferrin (TF), ferroportin, thioredoxin (TXN) and mitoferrin-2 by microarray and real-time qPCR in liver tissue. Gene expression of TF, catalase (CAT) and TXN were analyzed in control and hydrogen peroxide (H2O2) treated HepG2 cells by qPCR. Spearman’s rank correlation and Pearson’s product-moment were used for data analysis.

**Results:** Serum ferritin was significantly elevated in NASH vs. NC. In liver mRNA expression of the iron related genes was significantly elevated in NASH vs. NC (p<0.05). Analysis of gene expression data showed a positive correlation between both TF and CAT in NASH vs. NC. The mRNA expression of TF, CAT and TXN in cultured HepG2 cells was induced by H2O2 treatment (p<0.05) and a significant positive correlation was observed between TF and CAT and between TF and TXN.

**Conclusions:** The increased level of serum iron indices and iron related genes in NASH livers suggest an important role for iron in NASH. Further, the increased expression of iron related genes in HepG2 cells after an oxidative stress suggests a role for iron in the metabolism of H2O2 and hence in NASH.

**100 INTEGRIN BETA 8, BUT NOT BETA 5 OR 6, PROTEIN EXPRESSION IS INCREASED IN LIVERS OF CHILDREN WITH BILIARY ATRESIA.** Evan P. Nadler1, Christopher Rossi2, Robert Anders3, Kathleen Schwarz4, 1Surgery, Children’s National Medical Center, Washington, DC; 2Pathology, Children’s National Medical Center, Washington, DC; 3Pathology, Johns Hopkins School of Medicine, Baltimore, MD; 4Pediatric Gastroenterology, Johns Hopkins School of Medicine, Baltimore, MD

**Introduction:** Our previous work has shown that BA patients and a fibrotic gene signature show upregulation of integrin beta 5, 6, and 8 mRNA when compared to those with an inflammatory gene signature. To confirm whether mRNA upregulation translated into protein expression, we analyzed liver specimens from children with BA and normal and disease controls with the hypothesis that protein would be significantly increased in BA patients.

**Methods:** Liver specimens were obtained from infants with BA (n=17) and those who underwent biopsy for other diagnoses (n=11) from 2 collaborating institutions. Routine hematoxlyn and eosin staining and immunohistochemistry (IHC) for integrins beta 5, 6, and 8 was performed. A pathologist blinded to the treatment groups assessed fibrosis using Ishak scoring and scored IHC from 0-4 based on intensity of staining. Student’s t-test was used to compare the 2 groups with statistical significance assigned to p values < 0.05.

**Results:** Liver specimens from BA patients showed significantly more fibrosis than those from patients with neonatal hepatitis (n=6) or with normal liver tissue (n=5) based on Ishak score (2.3 ± 1.2 v. 0.5 ± 0.7, p <0.001). Similarly, integrin beta 8 staining was greater in BA patients when compared to controls (2.8 ± 0.9 v. 1.8 ±0.4, p =0.001). However neither integrin beta 5 (2.2 ± 1.2 v. 1.6 ±1.0, p =0.2) nor beta 6 (1.5 ± 1.0 v. 1.2 ±0.8, p =0.97) showed any difference between the 2 groups.

**Conclusions:** Integrin beta 8, but not beta 5 or 6, protein expression is increased in liver specimens from children with BA when compared to those from livers of healthy and disease controls. Fibrosis is also more significant in BA specimens. Further investigation into whether integrin beta 8, or this family of proteins as a whole may be attractive targets for future therapy in children with BA is warranted.
101 A SURVEY OF THE DIFFERENT MANAGEMENT PROTOCOLS FOR PEDIATRIC LIVER TRANSPLANTS. Catherine D. Newland, Matthew P. Tierney, J. M. Millis, Ruba Azzam, University of Chicago, Chicago, IL

Background: As newer immunosuppressant and antimicrobial medications have become available there has been a change in the care of post-liver transplant patients among different transplant centers. The purpose of this study was to determine the different post-liver transplant protocols used at pediatric liver transplant centers in the United States in regards to immunosuppression, antifungal, antibacterial and antiviral therapy and prophylaxis.

Methods: An electronic survey was emailed to pediatric hepatologists and liver transplant surgeons at 58 active pediatric liver transplant programs in the US and Canada. Responses were to be filled out by the person most knowledgeable about the post-liver transplant protocol and were collected from 2/26/2010 through 5/18/2010. The survey consisted of 39 questions which included the number of transplants performed annually, leading indications, different immunosuppressant agents, antimicrobials, and anticoagulation/antiplatelet agents used.

Results: Of the 146 recipients of the survey, 44 submitted responses. 24 completed the survey, 20 submitted incomplete surveys. The majority of centers performed 11-15 transplants per year and the leading indication was biliary atresia (83%). Induction therapy was used in 64% of responders. One hundred percent of participants use tacrolimus with a large range of variability for goal levels. Fifteen percent wean off calcineurin inhibitors after at least 2 years post-transplant. All (55%) who use antimetabolites use mycophenolate. All responders use corticosteroids with most using them for 6 months. Empiric antifungal prophylaxis is used by 56% of responders. Aspirin was used by 96% while 22% use heparin and 17% use Dextran-40.

Conclusion: There is an extremely wide range of variability in post-liver transplant management in US and Canadian centers. The results of this survey may provide guidance to clinical trial designs, quality assessment and improvement projects to optimize the different aspects of management of pediatric liver transplant patients.

102 THE SCENT OF NONALCOHOLIC FATTY LIVER DISEASE (NAFLD): ANALYSIS OF VOLATILE ORGANIC COMPOUNDS IN THE BREATH OF CHILDREN WITH FATTY LIVER.

Nishaben Patel1, Jonathan Moses1, Angela Shannon1, Ibrahim Hanouneh2, Katherine Melville1, Frank CiKach4, David Grove4, Stanley Hazen3, Raed Dweik4, Naim Alkhouri1,2, 1Pediatric Gastroenterology, Cleveland Clinic, Cleveland, OH; 2Digestive Disease Institute, Cleveland Clinic, Cleveland, OH; 3Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH; 4Respiratory Institute, Cleveland Clinic, Cleveland, OH

Background: Nonalcoholic fatty liver disease (NAFLD) is considered one of the most common serious complications of childhood obesity affecting approximately 10% of children. In the light of the increasing incidence of NAFLD and its implications, it is important to develop an easy and non-invasive diagnostic tool to detect patients with liver injury. Breath testing is becoming an increasingly important non-invasive diagnostic method that can be used in the evaluation of disease states. The aim of this study was to investigate the utility of volatile organic compounds (VOCs) measured by mass spectrometry to diagnose fatty liver in obese children.

Methods: Patients were recruited from the Pediatric Preventive Cardiology and Metabolic Clinic. All patients were screened with an ultrasound of the abdomen to evaluate for the presence of NAFLD. Exhaled breath was collected and analyzed per protocol using selective ion flow tube (SIFT-MS) to identify new markers of NAFLD.

Results: 44 patients were included in the study (25 with NAFLD on ultrasound and 19 with normal liver). All children were overweight or obese with a body mass index ≥ 85% for age. The mean age was 15± 3.1 years and 65% were female. AST, ALT and insulin level were significantly higher in patients with NAFLD. Patients with NAFLD to those without NAFLD revealed differences in concentration of more than 20 compounds. Further analysis revealed that breath isoprene, acetone, and trimethylamine were significantly higher in the NAFLD group compared to normal liver group (22.9±2 ppb vs. 14.5±1.5 for isoprene; 107.4±11.4 vs. 58.3±7 for acetone; 5.6±0.5 vs. 4.1±0.4 , p value < 0.05 for all). Conclusion: Exhaled breath analysis is a promising non-invasive method to detect fatty liver in children. Isoprene, acetone and trimethylamine are novel biomarkers that may help to gain insight into pathophysiological processes leading to the development of NAFLD. Future studies are needed to validate our findings.

103 A COMMON VARIANT IN PPARGC1A IS ASSOCIATED WITH NONALCOHOLIC FATTY LIVER DISEASE IN OBESE CHILDREN. Yu-Cheng Lin1, Pi-Feng Chang1, Yen-Hsuan Ni2, 1Pediatrics, Far Eastern Memorial Hospital, New Taipei City, Taiwan; 2Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

OBJECTIVE: There are substantial genetic components contributing to the susceptibility of non-alcoholic NAFLD disease (NAFLD). Recently, the single nucleotide polymorphism (SNP) in peroxisome proliferator activated receptor-γ coactivator-1α (PPARGC1A) gene was associated with NAFLD in adults. We aimed to test the hypothesis that PPARGC1A rs8192678 variant would increase the susceptibility of NAFLD in obese children.

METHODS: A total of 496 obese children aged 7-15 years were recruited. NAFLD was determined by ultrasonography. The SNP genotypes were detected by the 5’-Nuclease assay. Because PNPLA3 rs738409 variant was well known to confer susceptibility to NAFLD, we assessed the independent influence of PPARGC1A rs8192678 variant on NAFLD after conditioning on the effect of PNPLA3 rs738409 polymorphism.

RESULTS: 17.5% of the obese children had NAFLD. PNPLA3 rs738409 variants increase the odds ratio of NAFLD
104 DYSLIPIDEMIA AND METABOLIC SYNDROME IN CHILDREN AFTER LIVER TRANSPLANT. Emily R. Perito1, Sue Rhee1, John P. Roberts2, Philip Rosenthal1,2,1 Diagnosis: In adults after liver transplant, post-transplant metabolic syndrome (PTMS) increases cardiovascular disease—a leading cause of death in this group. In children after liver transplant, dyslipidemia is common but its clustering with hyperglycemia, obesity, and hypertension as PTMS has not been studied. Methods: Single-center, retrospective review of children <18 years who underwent liver transplant 1999-2011. Triglycerides (TG), HDL, LDL, cholesterol, weight, and blood pressures were classified with age and gender-specific guidelines. Children with ≥3 TGs >75th percentile, >30 days post-transplant, were classified as "elevated TGs." Hyperglycemia was ≥3 random glucose levels >200mg/dL. PTMS components included elevated TGs, hyperglycemia, low HDL (<10th percentile), overweight/obesity (BMI>85th percentile), and hypertension (>95th percentile). Results: Of 77 children included, 94% were on tacrolimus. 45% had persistently elevated TGs, with no difference in median follow-up after transplant by TG elevation (476 vs. 351 days, p=0.52). Children with elevated TGs were more likely to have hyperglycemia (37% vs. 5%, p=0.001) and other abnormal lipids: low HDL (n=14) 100% vs. 40%, p=0.04; high total cholesterol (n=15) 80% vs. 20%, p=0.03; high LDL (n=13) 67% vs. 10%, p=0.04). Those with elevated TGs were more likely to have other PTMS components at both 6 months (80% vs. 41%, p=0.001) and 12 months (80% vs. 38%, p=0.002) post-transplant. By 12 months, 43% of all children had ≥2 PTMS components. Conclusions: In this exploratory analysis, children with persistently elevated TGs after liver transplant were likely to have other PTMS components. Screening for PTMS may help identify children at-risk for long-term cardiovascular morbidity.

105 INCIDENCE OF ACUTE KIDNEY INJURY (AKI) FOLLOWING PEDIATRIC LIVER TRANSPLANT IN THE PERI-OPERATIVE PERIOD. James Squires, Kathy Campbell, Stuart Goldstein, John Bucuvalas, CCHMC, Cincinnati, OH
Calcineurin inhibitors (CNI) are the principal immunosuppressive medications used to prevent graft rejection and contribute to post-transplant kidney dysfunction. Additionally, acute kidney injury (AKI) is a predictor of mortality of patients in critical care units and leads to chronic kidney disease (CKD). Current literature suggests the 5 year incidence of CKD among pediatric liver transplant (LTX) recipients exceeds 20%. However, the prevalence of AKI in the peri-operative period in pediatric LTX recipients is not known. Furthermore, while patients with decreased GFR during the first month after LTX have increased risk for CKD, there is a paucity of longitudinal studies in which patients with AKI are rigorously identified. We hypothesized that AKI is prevalent in the immediate peri-operative period among pediatric LTX recipients. We conducted a single-center, retrospective cohort study of 21 consecutive pediatric LTX patients to determine the incidence of AKI as determined by the pRIFLE (Risk, Injury, Failure) criteria in the first 90 days after LTX. We found clear evidence of kidney injury in 28% (pRIFLE-Injury) of the cohort with 1% progressing to meet the definition of renal failure (pRIFLE-Failure). An additional 52% of the cohort developed pRIFLE-Risk. Interestingly, 19% of the cohort did not have evidence of evolving AKI over the 90 day observation period. Understanding the peri-operative incidence of AKI in the pediatric LTX population along with associated risk factors, combined with the knowledge that AKI increases the risk of long-term kidney dysfunction, would allow for both predictive and preventative measures that could significantly improve safety, short- and long-term outcomes for hospitalized children, especially those having undergone liver transplant.

106 HIGH PREVALENCE OF HBV NON-IMMUNITY IN VACCINATED PEDIATRIC LIVER TRANSPLANT RECIPIENTS. Matthew Ton-That1, Julie Economides3, Lekshmi Pillai2, Hyun Chul Lee2, Ryan W. Himes1,3, Daniel H. Leung1,3,1 Pediatric Gastroenterology, Hepatology, & Nutrition, Baylor College of Medicine, Houston, TX; 2 Baylor College of Medicine, Houston, TX; 3 Liver Center, Texas Children's Hospital, Houston, TX Background: Infections represent a significant threat in solid-organ transplant recipients. Behind influenza and pneumococcus, hepatitis B virus (HBV) claims more lives than any other preventable illness. HBV vaccine durability in the post solid-organ transplant setting has not been well studied. Methods: This was a prospective cross-sectional, single-center study evaluating HBV immunity in 117 pediatric
liver transplant recipients. Patients with hepatitis B surface antibody (anti-HBs) levels <10 mIU/mL were considered non-responders. Screening data included demographics, time since transplant, anthropometrics, albumin, WBC differentials, fat soluble vitamin levels, immunosuppression, and PELD/MELD scores.

Results: All 117 subjects received the full HBV vaccination series prior to transplant. 77 (65.8%) were non-immune. Among the non-responders, the mean anti-HBs level was 2.7 (±2.1) and among responders, 95.7 (±180.3). Older age (p=0.027), longer time since transplant (p=0.00001), and lower WBC (p=0.04) were associated with non-immunity. 50%, 66.7%, 77.8%, and 76.5% of children at ages 2, 3, 4, and 13-17 years, respectively, had non-protective anti-HBs. All other variables were not significantly different between immune and non-immune liver transplant patients.

Conclusions: This is the first U.S. study to prospectively evaluate the durability of hepatitis B immunity in pediatric liver transplant patients who were universally vaccinated prior to transplant. The majority of pediatric liver transplant patients were non-immune, beginning as early as age 2 years. Immunity rates from this study were lower than the recently reported 52-70% among immunocompetent 2-17 year old American children. Markers of nutrition and degree of immunosuppression were not predictors of non-immunity following vaccination. A systematic approach may be warranted to detect HBV vaccine non-responders among pediatric liver transplant recipients.

107 OUTCOME OF BILIARY ATRESIA SINGLE CENTER EXPERIENCE. George Yanni, Amul Shah, Manoj Shah, Marquelle Klooster, Trinh Truong, Khiet D. Ngo, Gilberto Bultron, Pediatrics, Loma Linda University Children’s Hospital, Loma Linda, CA

Background: Biliary Atresia (BA) is a destructive inflammatory oblitative cholangiopathy of neonates. Standard treatment following confirmed diagnosis is the Kasai portoenterostomy. Earlier reports suggested that children with BA who were operated on before 60 days old have better prognosis and outcome compared to children who were operated on after 60 days old.

The aim of our study is to report the LLUCH experience with children diagnosed with BA between January 1st, 1999 and December 31st, 2011.

Methods: Institutional Review Board permission was obtained. Charts of all children who were diagnosed with BA in our institution during the above time period were retrospectively reviewed.

Results: Thirty two children (13 males, 19 females) with BA were identified and assigned to 1 of 3 groups. Age at presentation was 17 days to 180 days. Group 1 includes 9 children who were diagnosed, and had their Kasai portoenterostomy (KP) before 60 days old. Group 2 includes 20 children who were diagnosed and operated on (KP) after 60 days old. Group 3 includes 3 children who were diagnosed after 90 days old, and underwent liver transplantation without KP. Outcomes: Group 1- 1/9 patients survives without complications, 4/9 patients underwent liver transplantation (1 died post transplant) and 4/9 developed portal hypertension and end stage liver disease (ESLD). Of these 4, 1 patient died while listed for transplant, 3 are waiting for liver transplantation. Group 2- 5/20 patients are alive without complications. 12/20 patients developed ESLD now doing well post liver transplantation, 3/20 patients developed ESLD and are on the waiting list for transplantation. Group 3- all patients are doing well post transplantation.

Conclusions: In our experience, timing of the KP did not correlate with the best outcome as previously reported. Children who were diagnosed >90 days old and underwent liver transplantation without KP have done well post transplantation.

108 EFFECTS AND RESULTS OF COUNSELING AND EDUCATING THE PATIENTS PRESENTING WITH HEPATITIS AT A TERTIARY CARE HOSPITAL. Sina Aziz1,2, Anoshia Raza1, Uzma Majeed1, Syeda Zauveen Ejaz1, Adeela Wahab1, Ushna Ashraf1, Shamsa Amin1, Pediatrics, DUHS, Karachi, Pakistan; 2Pediatrics, KMDC, Karachi, Pakistan

Background: Hepatitis is an escalating problem in Pakistan which needs immediate attention. Lack of awareness regarding the disease is contributing to its ever increasing frequency.

Objective: To assess and enhance the level of awareness regarding hepatitis amongst the patients presenting with hepatitis at a tertiary care hospital.

Methods: The research was conducted (under PMRC Grant No. 4-103-2/10/RDC/Dr.SJZ/DUHS/4481) at Civil hospital, Karachi. Only hepatitis positive patients participated. Each patient was required to fill in two standardized questionnaires. First questionnaire stated their level of awareness about hepatitis; followed by counseling. After six months a second, questionnaire assessed the benefits of counseling.

Results: Around 153 hepatitis positive patients were interviewed and counseled. Total of 153 patients participated, 108 females and 45 males. Out of them 83 had HCV, 56 had HBV, 08 had HBV plus HDV and 06 had HBV plus HCV. They received counseling on multiple parameters. Post counseling figures for patients using brand new syringes are (81%), screened blood for transfusion (81%), sterilized dental instruments (65.4%) and avoiding road side barbers (78.4%). The pre-counseling figures of the above mentioned parameters were 32%, 22.2%, 20.9% and 58.1% respectively. Patients and their family members were urged to get HBV vaccination. Post counseling, the
percentage of people who got themselves vaccinated increased from 3.2% to 36.6% and those who got their families vaccinated rose from 2.6% to 43.1%.

Conclusion: More awareness and counseling programs regarding hepatitis are needed in order to bring about a positive and a real change against the spread of this deleterious disease.

109 CHOLANGIOCARCINOMA IN A YOUNG WOMAN WITH PERINATALLY ACQUIRED HIV.

Henry C. Lin1,4, Richard Rutstein2,5, Joshua Cantor3, Sudha A. Anupindi4, Randolph P. Matthews1,5

1Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Division of General Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; 3Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA; 4Division of Radiology, Children's Hospital of Philadelphia, Philadelphia, PA; 5Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

We present a case of a 20 year-old HIV-infected woman who developed cholangiocarcinoma. The patient presented with acute onset of jaundice. She had been on antiretroviral therapy with poor adherence. Her CD4+ counts ranged from 100-150/mm³, with a CD4 percentage of 7-9%. On exam, the patient had scleral icterus but no hepatosplenomegaly. Labs showed a cholestatic hepatitis with synthetic liver dysfunction (total bilirubin 16.3 mg/dL, conjugated 1.4 mg/dL, AST 254 U/L, ALT 235 U/L, GGT 392 U/L, INR 2.22). Assays for other etiologies of hepatitis were negative. MRCP showed CBD stricture with gradual tapering of the distal CBD and beading of the liver was performed with subsequent Roux-en-Y hepaticojejunostomy to the left hepatic duct. A negative tumor margin was achieved. Light microscopy showed a poorly differentiated cholangiocarcinoma with focal areas of necrosis, lymphovascular invasion, and perineural invasion. All submitted lymph nodes were negative for carcinoma. CA 19-9 level was elevated (30 units/mL). Postoperatively, adjuvant chemotherapy (Gemcitabine) was administered. The most recent MRI showed no intrathoracic metastasis. For continued treatment, she is on an antiviral regimen of Darunavir, Ritonavir, and Raltegravir.

110 NOVEL TARGETS OF THE MIR-30A FAMILY, REGULATORS OF BILE DUCT DEVELOPMENT.

Claire Le Guen, Nicholas J. Hand, Joshua Friedman, Pediatrics, Division of Gastroenterology and Nutrition, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

MicroRNAs are single stranded, non-coding, endogenous RNA molecules that regulate gene expression. The miRNAs miR-30a and miR-30c2 have been identified in the ductal plate and bile ducts and are linked to vertebrate hepatobiliary development. However, the genes that they target have not been fully elucidated.

In this study, we used dual luciferase reporter assays to test predicted targets of the miR-30 family. Reporter plasmids coupling the 3'UTRs of the predicted target genes to the renilla luciferase gene were used to monitor miRNA:target interaction. We modified the standard reporter plasmid to include a weaker promoter (PGK) to emulate physiological expression and facilitate miRNA regulation. Functional levels of the miRNAs were manipulated in four ways: repression was increased by overexpression of the miRNAs, or decreased by overexpression of either artificial mRNA containing tandem arrays of target sites ("miRNA sponges") or bulged hairpin miRNA binding sites ("tough decoys") or by using antisense oligonucleotides. Using gene expression arrays we previously profiled the miR-30 target transcriptome in a hepatoblast cell line and identified candidate direct targets of potential interest in hepatobiliary development using computational prediction algorithms. These include: Smad1 (signaling), Celsr3 (cell polarity), and Ccne2 (cell growth).

Using the modified reporter assay, ten of eleven miR30a/c2 predicted targets previously identified as non-targets using the traditional reporter were validated as true targets. Several of these have functional implications for the growth and differentiation of bile ducts. These results also reveal that miRNA and target expression must be expressed at appropriate levels to accurately detect miRNA regulation.

111 LIVER ABSCESS IN COLOMBIAN CHILDREN.

Carlos A. Velasco-Benitez, Ana R. Guzman-Benavides, Universidad del Valle, Cali, Colombia

Introduction: Liver abscess (LA) in developing countries, is presented at an early age. Objective: To describe children with clinical (triad fever, hepatomegaly and right upper quadrant pain) and paraclinical (abdominal ultrasound: AU) diagnosis of LA in the Hospital Universitario del Valle de Cali, Colombia. Methodology: We collected data from medical records of 14 children under 15 years of age with diagnosis of LA. We analyzed sociodemographic, clinical and paraclinical variables. Results: Age 8.7 years of age with first time diagnosed, 7 male, with a median time of 13.5 days and median hospital stay of 21.7 days. Other symptoms included vomiting, anorexia, diarrhea, cough, headache and asthenia. Global malnutrition showed 5/7. The AU were located LA on the right, being unique in 11/13. Other paraclinical showed: hypoalbuminemia, increased ESR and CRP, and impaired liver function tests. In
9/14 children's material culture collection identified drainage mainly E. coli, S. viridans, and S. epidermidis. 3/6 presented amoebas to stool examination. Median medical management lasted was 17.7 days, with antibiotics such as oxacillin, clindamycin, metronidazole, amikacin, ceftriaxone, cefotaxime, ampicillin-sulbactam, piperacillin-tazobactam, metronidazole. 9/10 required surgical drainage guided by ultrasound. Conclusion: The LA should be suspected clinically with the triad fever, hepatomegaly and right upper quadrant abdominal pain, verify their location and type of presentation with an abdominal ultrasound, supporting some paraclinical diagnosis with blood and feces, and initiate a prompt and suitable worming and medical treatment with appropriate antibiotics following developments, thereby avoiding the complications that can lead to increased morbidity and mortality.

1Vanderbilt Children's Hospital, Nashville, TN; 2Salford Royal, Salford, United Kingdom; 3Central Manchester, Manchester, United Kingdom; 4Kings College Hospital, London, United Kingdom; 5University of Minnesota, Minneapolis, MN; 6New York Presbyterian, New York, NY; 7Northshore-LIJ, Manhasset, NY; 8University of Turin, Turin, Italy; 9The Hospital for Sick Children, Toronto, ON, Canada; 10UCLA, Los Angeles, CA; 11Instituto Giannina Gaslini-Ospedale Pediatrico, Genova, Italy; 12Stanford University, Palo Alto, CA; 13Children's Hospital Pittsburgh, Pittsburgh, PA; 14Ain Shams University Hospitals, Cairo, Egypt; 15Synageva BioPharma, Lexington, MA

LAL Deficiency is a rare autosomal recessive disorder caused by mutations in the LIPA gene encoding lysosomal acid lipase, a key enzyme in lysosomal processing of cholesterol esters and triglycerides. Markedly reduced LAL activity results in accumulation of lipids in various tissues, causing malabsorption, hepatosplenomegaly, liver failure, and growth failure. The early onset form (Wolman disease), is progressive and typically manifests in the first few months of life. Demographic and clinical information on 28 patients (16 males, 12 females) have been collected utilizing clinical chart data abstractions. This report focuses on 19 patients with growth failure by 6 months of age. The median age (range) at first symptom, diagnosis, and death were 1 month (0.23 - 3), 2.17 months (1.05 - 7.07), and 3.44 months (1.45 - 37.37), respectively. Six of these patients had hematopoietic stem cell (n=5) or liver transplants. Excluding these 6 patients, the median age (range) of death was 2.95 months (1.45 - 5.72). Of the 6 transplanted patients, 5 died before 9 months of age, while the 6th, the liver transplant recipient, died at 37.37 months. Six of 18 patients (33%) did not have adrenal calcifications. We conclude that the clinical course of early onset LAL Deficiency is rapidly progressive leading to near certain death during the first year of life.

Cellular/Molecular Biology

113 INDUCED PLURIPOTENT STEM CELL MODEL TO STUDY EFFECTS OF JAG1 MUTATION IN ALAGILLE SYNDROME. Henry Lin1,2, Ellen A. Tsai3, Deborah McEldrew1, Paul Gadue1, Nancy B. Spinner2,4,1Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Department of Pediatrics, University of Pennsylvania, Philadelphia, PA; 3Genomics and Computational Biology Graduate Group, University of Pennsylvania, Philadelphia, PA; 4Department of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia, Philadelphia, PA

Separation of cell types from the mosaic individual allows for gene expression analysis to investigate the effects of the alteration alone. We have studied a patient with Alagille syndrome (ALGS) with a mosaic deletion of chromosome 20 that includes the JAG1 gene. ALGS is an autosomal dominant, multi-system disorder with variable penetrance caused by JAG1 or NOTCH2 mutations. The liver phenotype of ALGS has been difficult to model in animals.

We have established induced pluripotent stem cells (iPS cells) from patient fibroblasts with and without a JAG1 deletion. Fibroblasts were dedifferentiated into iPS cells using an established four-factor polycistronic lentiviral construct. Individual iPS cell lines, JAG1 deletion and wildtype (WT), were isolated through the cloning process. We also established fibroblasts with and without a JAG1 deletion by dilution plating, to study gene expression in the fibroblasts, for comparison to the iPS cells. To determine the downstream targets of JAG-NOTCH signaling, the JAG1 deletion and WT lines were differentiated into three distinct cell stages: stem cell, endoderm, and early hepatocytes. RNA expression analysis is being performed using Gene ST microarrays to compare differential gene expression between JAG1 deletion and WT cells at each cell stage. Genesthat are differentially expressed will be further studied to understand their role in the NOTCH signaling pathway, and they will be evaluated as candidate genes for a role in liver disease associated with ALGS. A goal of this work is to test these genes for a role as modifiers of liver disease severity in ALGS. In conclusion, iPS cells can be generated from patient fibroblasts, providing a mutation specific disease model.
**114 ABSENCE OF CORRELATION BETWEEN RS3761547 FOXP3 POLYMORPHISM AND CELIAC DISEASE.** Gloria Serena, Alessio Fasano, Craig Sturgeon, Mucosal Biology Research Center, University of Maryland, Baltimore, MD

Background: Celiac disease is an autoimmune enteropathy triggered by the ingestion of gluten in genetically predisposed individuals. FOXP3 is the master regulator for the development and suppressive function of regulatory T cells, a minor subpopulation of T cells involved in regulation of immune response, maintaining immunological self-tolerance and immune homeostasis, including control of autoimmune diseases and cancer surveillance. Polymorphisms in foxp3 gene have been associated to several autoimmune diseases as autoimmune thyroid disease and systemic lupus erythematosus. The presence of polymorphisms in foxp3 gene could potentially alter the FOXP3 function and therefore potentially related to celiac disease onset. Aim: To detect potential correlation between foxp3 gene polymorphisms and the onset of celiac disease.

Methods: DNA extracted from 6 celiac and 8 control patients was amplified by PCR. The foxp3 gene was then entirely sequenced and the obtained sequences compared with the foxp3 sequence in GENE BANK. From this screening analysis we were able to select one point mutation that seemed to be potentially associated with celiac disease (rs3761547), a polymorphism already associated with allergic rhinitis. We then proceeded with the specific screening for this polymorphism in 23 controls and 47 celiac patients.

Results: The initial screening showed 50% of the celiac patients presenting the polymorphism rs3761547 while none of the controls presented it. These results lead us to screen a larger number of patients and controls for that specific polymorphism. This expanded analysis failed to reveal any difference between celiac patients and controls, with 20% of both controls and celiac patients showing the polymorphism. Conclusions: In this study we performed a screening of the entire foxp3 gene in order to detect polymorphisms potentially associated with the celiac disease onset. Our analysis didn't reveal any association between celiac disease and the presence of polymorphisms excluding a possible association of celiac disease with point mutations in foxp3.

**115 HAPTOglobIN GENOTYPES IN INFLAMMATORY DISORDERS.** Craig Sturgeon, Anna Sapone, Debora Angrisani, Dario Siniscalco, Amalia Cirillo, Laura De Magistris, Alessio Fasano, School of Medicine, University of Maryland, Baltimore, MD; Department of Experimental Medicine, Second University of Naples, Naples, Italy

Intestinal permeability has recently been implicated in many inflammatory disorders including celiac disease, type-1 diabetes, autism, inflammatory bowel disease, and asthma. Zonulin is a major regulator of intestinal permeability and is overexpressed in celiac disease and diabetes. We have described zonulin to be the precursor to haptoglobin 2 (Hp2). Prior to our identification of zonulin as Hp2, haptoglobin genotypes have been shown to be associated with many disorders. We therefore explored the distribution of haptoglobin genotypes in inflammatory disorders.

We genotyped a total of 224 celiac, 138 T1D, 50 Sjogrens and 41 autistic patients. We compared these results to previously published controls. The controls had a genotype distribution of 16.5% Hp1-1, 48.3% Hp2-1 and 35.0% Hp2-2. The genotype distribution for celiacs is 13.4% Hp1-1, 42.0% Hp2-1, and 44.6% Hp2-2. The genotype distribution for diabetics is 20.3% Hp1-1 49.3% Hp2-1, 30.4% Hp2-2. The genotype distribution for Sjogren's disease is 18.0% Hp1-1, 46.0% Hp2-1, and 36.0% Hp2-2. The genotype distribution for Autism is 9.8% Hp1-1, 56.1% Hp2-1, and 34.1% Hp2-2. Only the genotype distribution for celiacs reached statistical significance (p<0.01). There was no difference for T1D or Sjogren's disease patients. While the distribution for autism did not reach statistical significance there is still a shift of genotypes away from Hp1-1. Combined these data show that both celiac disease and autism show a shift away from the Hp1-1 genotype, while only celiac disease shifts toward Hp2-2. Both T1D and Sjogren's patients show similar distributions to controls.

**Motility/Functional Gastrointestinal Disorders**

**116* CONSTIPATION AND FECAL INCONTINENCE: EFFECTS ON QUALITY OF LIFE.** Alan H. Silverman, Suzanne Mugie, Carlo DiLorenzo, Samuel Nurko, Rina Sanghavi, Anand Ponnambalam, Pippa Simpson, Mana R. Sood, Medical College of Wisconsin, Milwaukuee, WI; Nationwide Children's Hospital, Columbus, OH; Children's Hospital of Boston, Boston, MA; UT Southwestern Medical Center, Dallas, TX; University of South Alabama Children's and Women's Hospital, Mobile, AL

Background: Children with constipation (C) have lower quality of life (QoL) than children with IBD, GERD and healthy controls. Children with fecal incontinence (FI) have reduced emotional/social functioning. The purpose of this study was to assess effects of C with and without FI on QoL. Method: Families of children with ROME III criteria for C were consented for this study. Data was collected in five children's hospitals. Families completed a demographic form, QoL measures, functional disability measures, and general psycho-social functioning measures. All children under 4 years of age were classified as C only. Results: Families of 440 children ages 2-17 years (SD=3.7 years) completed questionnaires (53% male). 184 children had C alone, 226 children had C-FI, 14 children had C-IBS, and 14 had FI alone. Approximately 50% of the sample reported difficulty or failure to achieve toilet training for bowel movements. Another 40% reported FI multiple episodes weekly. Severity of FI was negatively associated with measures of QoL including measures of family impact, measures of Parent QoL, and a measure of
general QoL (all p values <0.001). Older children tended to have lower QoL than younger counterparts (p <0.001). Severity of FI was associated with the physical function problem scale, and the measure of general functioning (p values <0.01). Frequency of soiling was associated with only functional disability. Conclusion: This multicenter study suggests that children with C have lower QoL compared to healthy peers. Children with FI have worse QoL, and with increasing severity of FI there was deterioration in physical functioning and general functioning. Parents and family QoL is also adversely affected by FI. Strategies for early intervention to tackle FI may mitigate the psychological sequela.

117* BALLOON EXPULSION TEST AS A SCREEN FOR OUTLET OBSTRUCTION IN CHILDREN WITH CHRONIC CONSTIPATION. Jaime Belkind-Gerson\textsuperscript{1}, Alan M. Goldstein\textsuperscript{2}, Brad Kuo\textsuperscript{3}
\textsuperscript{1}Pediatric GI, Massachusetts General Hospital, Boston, MA; \textsuperscript{2}Pediatric Surgery, Massachusetts General Hospital, Boston, MA; \textsuperscript{3}GI Unit, Massachusetts General Hospital, Boston, MA
Chronic constipation (CC) is a common problem in pediatrics and is often the result of obstructed defecation. Objective: To study the feasibility and efficacy of the balloon expulsion test (BET) in the diagnosis and management of children with CC. Methods: Retrospective study comparing BET and High-Resolution Anorectal manometry (ARM). The BET was done together with ARM in 29 children 8-19 with CC. For BET a 60ml balloon was used. Passage of balloon in 1 minute or less was considered normal. Results: Fifteen of the 29 children had a normal BET. Of these, 14 also had an ARM, all of which were normal (except for two cases with a hypertonic baseline anal sphincter). Thus 12 of 14 with BET and ARM were normal on both (correlation between the tests = 86%). Of the 14 children that failed BET, 10 had distal abnormalities by ARM, contrast studies, EMG or assessment by a pelvic physical therapist. All patients with a non-relaxing sphincter or outlet obstruction were treated with laxatives, anal sphincter Botox and/or pelvic physical therapy and biofeedback. In follow-up of at least 3 months, all patients with a failed BET were improved. Conclusions: We found a high correlation between a normal ARM and BET. If the BET is abnormal and the ARM does not identify a cause for the distal obstruction, additional studies may be needed, including contrast enema, defecography, or EMG. BET appears to be a safe, reliable and useful test in the evaluation and management of CC in children.

118* BEAR-DOWN MANEUVER (SIMULATED DEFCATION) USING AIR INSUFFLATION, DURING HIGH-RESOLUTION ANO-RECTAL MANOMETRY IN CHILDREN AND ITS CORRELATION TO THE BALLOON EXPULSION TEST. Jaime Belkind-Gerson\textsuperscript{1}, Brian Surjanhata\textsuperscript{2}, Brad Kuo\textsuperscript{3}, \textsuperscript{1}Pediatric GI, Massachusetts General Hospital, Boston, MA; \textsuperscript{2}GI Unit, Massachusetts General Hospital, Boston, MA
Introduction: Dysynergic defecation is common in constipated adults and children, but its mechanisms are difficult to study. The balloon expulsion test (BET) is helpful but does not explain the mechanistic defect. The bear-down maneuver (BDM) during anorectal manometry (ARM) is used in adults but has not been studied in pediatrics. Aims: To investigate if BDM in chronically constipated (CC) children correlates with BET and if it provides additional clinically important information. Methods: Retrospective review of 30 CC children (8-19 yrs) (Rome 3) with ARM and BET. Normal BET: 60ml balloon passed ≤60 sec. The BDM done with 0, 20, 40 and 60 ml of air in balloon while measuring recto-anal pressure differential (RAPD) (rectal pressure - anal resistance). Results: During BDM: 1) In all, anal sphincter pressure (ASP) was sig lower at 20, 40 or 60 ml vs 0 ml of inflation. 2) In pts with nl BET, ASP was sig lower vs pt with abnl BET at 60 mL only. 3) In all, the Rectal Pressure (RP) was sig higher at 20, 40 or 60 ml vs 0 ml. 4) In pts with nl BET, RP was sig higher vs to abnl BET pts during BDM at all inflations except 0 mL. 5) At 60 ml a positive value for RAPD was able to predict nl BET with: sens 83%, spec 78%, PPV 71%, NPV 88%. Conclusions: 1) Dynamic testing using BDM with balloon inflation in pediatrics gives better insight of pathophysiology of outlet obstruction by examining the RP and ASP. 2) Pts that have nl BET tend to have decreased ASP and increased RP versus pts with abnl BET. 3) BDM at 60 mL may be best, due to significantly lowered ASP versus all inflations and the good sensitivity and specificity when compared to BET. 4) When the RAPD (RP-ASP) is a positive value, defecation mechanisms will usually be adequate and patient will have a normal BET. 5) The information obtained during BDM may be valuable for planning pelvic training/therapy as well as anal Botox use. 6) The BDM test can be done in children 8 yo or older.
119* EFFECTS OF GDNF AND ENDOTHELIN-3 ON ENTERIC NEURAL STEM CELL PROLIFERATION AND DIFFERENTIATION. Alfonso Carreon-Rodriguez1,2, Alan M. Goldstein2, Jaime Belkind-Gerson1,2, 1Pediatric GI, Massachusetts General Hospital, Boston, MA; 2Pediatric Surgery, Massachusetts General Hospital, Boston, MA.

Background: Enteric neural stem cells (ENSC) present in embryonic and postnatal rodent and human intestine may be useful in cell therapy for intestinal neuropathies. Aim: To study the capacity of ENSC to proliferate and differentiate in vitro in response to GDNF and Endothelin-3 (ET3). Materials & Methods: Single E14 rat intestine cells grown as neurospheres (NS) in proliferation with EGF and bFGF and treated with GDNF and ET3 alone and together. After 7 days, NS morphology, number and size were recorded. NS were dissociated and replated with GDNF, ET3 or both: a) at clonal density in collagen in proliferation for 21 days or b) in differentiation for 7 days. After treatment, colony morphology, number and size were recorded. Neuronal differentiation was investigated by TuJ1 immunoreactivity. Results: 1) In initial cultures GDNF produced NS >2 mm vs. control NS <0.5 mm. ET3 did not increase NS size vs. control, but yielded a 70% increase in NS number. 2) Cells in collagen grew only with GDNF, giving rise to colonies >2 mm with ~10,000 cells. These NS gave rise to new NS upon replating in proliferation conditions. 3) In differentiation, GDNF produced the largest colonies, with longer and thicker extensions, while ET3 generated smaller colonies with shorter and thinner extensions vs. control or GDNF. Cells with GDNF and ET3 produced intermediate size and neurite length colonies. 4) Tuj1+ cells were found in control and GDNF-treated cells in the differentiation phase. Conclusions: 1) Primary cultures of rat embryonic intestine are an excellent model for NS development, giving rise to colonies capable of self-propagation and neuronal differentiation, consistent with stem cell behavior. 2) GDNF stimulates both proliferation and differentiation of ENSC to form large neural colonies with elongated neurites. 3) ET3 stimulates proliferation of ENSC but prevents neuronal differentiation.

120 LONGITUDINAL AND RADIAL CHARACTERISTICS OF INTRA-ANAL PRESSURES USING 3-D HIGH-DEFINITION ANORECTAL MANOMETRY. Lusine Ambartsumyan, Leonel Rodriguez, Claudio Morera, Samuel Nurko, Gastroenterology, Boston Children's Hospital, Boston, MA

Background: The pathophysiology of fecal incontinence is not well understood. Standard or High resolution anorectal manometry (ARM) provide simple two-dimensional (2D) intra-anal pressure measurements and do not identify radial asymmetry or localize abnormal sphincter function. 3-D high-definition anorectal manometry (HDARM) has 256 pressure sensors distributed circumferentially and provides a detailed topographical and three-dimensional pressure gradient representation of the anal canal. The aim of the present study was to use HDARM to characterize intra-anal pressure profiles in children. Methods: HDARM manometric tracings of 20 children with functional constipation referred for anorectal manometry were reviewed. 2-D pressure profiles using high resolution manometry were used to measure the length of the internal anal sphincter (IAS). The IAS was divided into four equal segments from the anal verge to adjust for variable sphincter length. Longitudinal and radial measurements of sphincter pressure during rest (anterior, left, posterior, right walls of IAS) were taken along each segment in 2D and 3D topographical views. A 3D reconstruction was constructed. Results: Mean age was 12.7 ± 3.6 years and mean IAS length was 3 ± 0.8 cm. Using 2-D manometry the mean peak IAS pressure was 74 ± 19 mmHg, and was located between the 1st and 2nd segment of the IAS. 3-D demonstrated both longitudinal and radial asymmetry along the anterior, left, posterior, and right walls of the IAS. Anterior pressures were significantly lower than posterior pressures longitudinally and radially in segments 2 (61±25 vs. 84±24), 3 (43±24 vs. 75±23), and 4 (22±18 vs. 44±18)(paired t-test, p<0.05). Conclusion: 3-D HDARM allows for a detailed characterization of intra-anal pressures. 3D topographic pressure measurements demonstrate longitudinal and radial asymmetry of the IAS. This is the first time radial asymmetry of the IAS has been described in children. 3-D HDARM may allow for a better understanding of fecal incontinence after anal surgery for congenital malformations.

121 MOTILITY DISORDERS, THE RESULT OF AN AUTONOMIC DYSFUNCTION? Gisela Chelimsky1, Christina Gorges1, Tom Prieto2, Manu R. Sood1, 1Pediatrics, Medical College of Wisconsin, Milwaukee, WI; 2Neurology, Medical College of Wisconsin, Milwaukee, WI

Background: Reports of the relation between motility disorders and autonomic nervous system dysfunction are scarce, focused mainly on autoimmune disorders and pseudo-obstruction. Hypothesis: Neuropathic pseudo-obstruction in children is associated with autonomic neuropathy. Methods: Retrospective IRB approved review of all charts between 4/02 and 4/12 of children ages 5 to 18 who underwent antroduodenal motility (AD) or colonic motility (CM) for significant concerns about dysmotility and had autonomic testing performed (deep breathing DB, Valsalva maneuver VM, tilt tables test and sudomotor axon reflex tests). Results: 19 subjects were reviewed, 13 females. Mean age at time of motility study of 14.4 +/- 3.3 yrs. 12 subjects underwent AD motility and 13 CM. 42% showed postural tachycardia syndrome (POTS-Heart rate increase > 35
Abstracts

E36

bpm with associated orthostatic symptoms). Five percent had orthostatic hypotension. 21% had an abnormal DB or VM. 31% had an autonomic neuropathy (≥ 2/4 sites with <50% lower limit sweat output).

Conclusions: A small group of children with significant motility disorder have an autonomic disorder. Therefore, autonomic testing should be considered in all children with documented dysmotility. The autonomic testing results may aid in the evaluation and treatment of these children. This study underscores the need for prospective studies comparing autonomic dysfunction in healthy subjects and subjects with presumed motility disorders and perhaps evaluation of the heart rate variability to determine the sympathetic/parasympathetic tone.

<table>
<thead>
<tr>
<th></th>
<th>No POTS</th>
<th>POTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal AD motility</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal AD motility</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Normal colonic motility</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal colonic motility</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No neuropathy</th>
<th>Neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal AD motility</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal AD motility</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Normal colonic motility</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal colonic motility</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

122 PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS MORE THAN 1000 CHILDREN AND COUNTING. Miguel Saps1, Carlos A. Velasco-Benitez2, Diana Nichols-Vinueza2
1Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2Universidad del Valle, Cali, Colombia
Pathogenesis of functional gastrointestinal disorders (FGIDs) is unclear. Genetic, environmental and psychosocial factors thought involved. Factors change by culture, society, country and region. Learning how factors influence FGIDs epidemiology may help understand pathogenesis and optimize resources. Functional International Digestive Epidemiological Research Survey (FINDERS) is an unfunded voluntary international collaborative task group created to assess FGID epidemiology in 10 Latin-American countries. FINDERS currently collecting in 3 countries (South, Central America). We present data from ongoing Colombian section (goal 2500 children various socioeconomic levels, 10 cities, different sizes, climate, economy). Cucuta and Barranquilla data is under analysis. AIM: International epidemiology of FGIDs. METHODS: 1234 children from private and public schools 11.4±2.2 years (8-19) of age (58.9% M), 3 cities in Colombia (Pasto population 400.000, Cali 2.120.000, Bogota 6.840.116). English version of Questionnaire of Pediatric Gastrointestinal Questionnaire (QPGS) (Rome III criteria) translated by FINDERS with reverse translation according to international standards. Validation measures of Spanish version were done. Children trained on QPGS completion by research team. Private completion. 332 children had FGIDs (26.9%). Functional constipation (FC) was the most common FGID in 3 cities (14.4% each gender). Abdominal pain (AP)-FGIDs diagnosed in 10.4% (M 9.35%, F 11.8% p=0.19) of children (11.4±2.2 years). IBS- most common AP-FGID followed by functional AP. CVS, rumination and non-retentive fecal incontinence uncommon in 3 cities (<0.01%). DISCUSSION: The largest multicenter FGIDs prevalence study ever performed in Latin America in school children. Despite distance, different sociocultural and genetic backgrounds, FGIDs prevalence is grossly similar to distant countries. CONCLUSION: FGIDs are common in Colombian children. Functional constipation is the most common functional disorder.

123 VALIDATION OF THE ROME III CRITERIA. HIGH INTERNAL CONSISTENCY OF THE QUESTIONNAIRE OF PEDIATRIC GASTROINTESTINAL SYMPTOMS (SPANISH VERSION)
Carlos A. Velasco-Benitez2, Diana Nichols-Vinueza2, Alejandro Castillo3, Miguel Saps1
1Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2Universidad del Valle, Cali, Colombia; 3Fundacion Valle del Lili, Cali, Colombia
There is little validation of the Rome III criteria (RC). IC measures the correlations between different items on the same diagnostic instrument (i.e. RC). Testing IC of the RC is relevant in the process of validation. There are no studies on IC of the RC. The QPGS-III is an age appropriate instrument designed to diagnose functional gastrointestinal disorders according to RC. Aim: To determine IC, stability and equivalency of the Rome criteria. Methods: QPGS-III was translated form English into Spanish with reverse translation into English following standard principles. 1234 school children (mean 11.4±2.2 years, range 8-19, male 55.7%) from two public and 4
private schools from 3 cities in Colombia: Bogota (154), Cali (738) and Pasto (342) were given the 71 questions of the QPGS-III. The 4 sections of the QPGS-III: A- supraumbilical pain and discomfort; B-umbilical, periumbilical and infraumbilical pain and discomfort; C-bowel movements; D other digestive symptoms, were analyzed for internal consistency using Cronbach alpha, a statistical test that calculates the pairwise correlations between items (0-1 range). Results: The initial and final English texts were compared by 4 raters and showed good agreement with the original version and the questionnaire was easy to complete and understand. The Cronbach's alpha was: 0.9316; section A: 0.9117; section B: 0.9301, section C: 0.9301 and section D: 0.7315. The high level of IC shown in this study indicates that the criteria measure a single unidimensional latent construct and that there is high correlation between the different items in the criteria. Conclusion: The Spanish version of the QPGS-III has high IC and the questions were found easy to understand by Colombian Spanish speaking children.

124 PREVALENCE OF ABDOMINAL PAIN (AP) RELATED FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDs) IN PEDIATRIC RECIPIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT). Miguel Saps, Larisa Broglie, Karina Danner-Koptik, Sonali Chaudhury, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL
Consultation for AP on pediatric HSCT recipients is common. GI graft versus host disease (GVHD) and infectious complications are common in HSCT. GI inflammation (infectious and non-infectious) has been associated with postinflammatory (PI) AP-FGIDs. PI-AP-FGIDs usually improve with time (months/ years). The presence of AP-FGIDs in HSCT recipients has never been described. Aim: Assess prevalence of AP and AP-FGIDs in pediatric HSCT recipients. Hypothesis: 1-AP-FGIDs are frequent after HSCT. 2- AP-FGIDs frequency will decrease with time from HSCT. Methods: Parents of children who had HSCT (allogeneic and autologous) > 2 years earlier, followed in clinic and had no recent GI infection/active GVHD completed the Questionnaire of Pediatric Gastrointestinal Symptoms (AP characteristics and FGIDs diagnosis). Results: 44 HSCT children, 59.1% males, mean age 10.2 years (range 5-17). Caucasian 59.9%, African-American 15.9%, Hispanic 11.3%, Asian 4.5%, 8.4% unknown. Average time interval from HSCT: 72.11 months (range 31-142). AP reported: 7/44 (15.9%). Mean age HSCT recipient with AP: 9.7 years (3-15) vs. 10.4 years (4-17) in no AP. AP-FGIDs diagnosed in 3 (IBS, functional AP, dyspepsia). Indications for HSCT in AP group: Acute Lymphoid Leukemia (2), Neuroblastoma, Anaplastic Lymphoma, Acute Myeloid Leukemia, Hypereosinophilic Syndrome and Chronic Granulomatous Disease. Time interval from HSCT in AP group: mean 47.7 months, median 48 months (range 31-75); time interval from HSCT in no-AP group: mean 76.9 months, median 69 months (range 32-171), p= 0.029. 3/7 AP group had GVHD or GI infections after HSCT. Conclusions: AP-FGIDs are common after HSCT in children. AP was more frequent in patients with shorter interval from HSCT. Study suggests that post-HSCT AP-FGIDs course is similar to other inflammatory GI conditions. Large studies should confirm findings. The investigation of post-HSCT AP-FGIDs may help understand pathogenic factors of FGIDs including role of inflammation, stress, coping and families.

125 RELATIONSHIPS BETWEEN PARENTAL PROTECTIVE BEHAVIORS AND CHILD QUALITY OF LIFE AMONG CHILDREN WITH CHRONIC ABDOMINAL PAIN. Emily D. Kessler1,2, Michael C. Roberts1, Jennifer V. Schurman2, 1University of Kansas, Lawrence, KS; 2Children's Mercy Hospitals & Clinics, Kansas City, MO
Background. Interaction with parents is one psychosocial factor of particular interest in understanding pediatric chronic abdominal pain (CAP) from a biopsychosocial framework. Protective behaviors are among the most common parental responses to child pain, perhaps due to their intuitive appeal. However, initial studies have documented associations between parental protective behavior, broadly defined, and child somatic complaints, emotional difficulties, and functional disability. This study builds upon previous research by examining two distinct types of protective behaviors (i.e., provision of attention, release from daily responsibilities) in relation to the broad construct of quality of life (QoL) among children with CAP. It also attempts to clarify a somewhat mixed literature regarding the moderating effects of age and gender on relationships between parental protective behaviors and child functioning. Methods. Medical records for all patients (8-17 years) evaluated in a multidisciplinary abdominal pain clinic over a 3-year period (n=440) were reviewed. Parent-reported attention (ATTN) and release from responsibility (RFR), as well as child- and parent-reported physical and psychosocial QoL, were assessed as part of routine care. Results. RFR significantly predicted child QoL in all regression models. ATTN interacted with RFR to predict parent-reported QoL. Age interacted with both ATTN and RFR to predict psychosocial, but not physical, QoL; however, the effect of age was not consistent across reporter. No gender differences emerged. Conclusions. Results indicate that ATTN and RFR have unique, and interacting, relationships with child QoL. Clinically, the combination appears most problematic. In terms of age, RFR appears to have a stronger negative relationship with QoL for adolescents than younger children. The effect of age on the relationship between ATTN and QoL, however, varied by domain and reporter; further examination may help clarify this complex relationship.
126* CYCLIC VOMITING SYNDROME (CVS) OFTEN RESPONDS TO MIGRAINE BASED THERAPY. Caroline Jeon¹, Robert Issenman², ¹Michael G. DeGroote School of Medicine, McMaster University, Hamilton, ON, Canada; ²Division of Pediatric Gastroenterology, McMaster University and McMaster Children's Hospital, Hamilton, ON, Canada

Introduction: CVS is a condition characterized by repetitive bouts of intense nausea and vomiting interspersed with interval return to normal state. As many children go on to develop recognizable migraine headache, our centre has adapted an approach borrowed on evidence-based migraine therapy. Parents and children are taught early recognition of a prodrome and use of NSAIDs and a prokinetic drug (domperidone) to abort incipient attacks. Nutritional strategies are recommended to avoid food triggers as well as hypoglycemia at night and during exertion. Methods and Population: A single centre chart review includes 73 children with CVS diagnosed according to standard criteria seen between 2006 to present for whom follow-up was available. Mean age was 12. There were 39 males. On average children were diagnosed at age 8.7. The duration of attacks ranged from 2.5 hours per episode to days. Improvement was defined as complete resolution of symptoms or 50% improvement in number or duration of attacks.

Results: Upon analysis, 55 out of 73 total patients had a measurable outcome. Of these, 10 patients received the standard intervention, and 31 received migraine based intervention. From these, 25 out of 31 patients (80%) treated with the McMaster protocol showed improvement, whereas 4 out of 10 patients (40%) receiving the standard intervention improved (p<0.05).

Conclusion: CVS comprises a heterogeneous group of conditions whose pathogenesis is not fully understood. However, in this population symptoms resolved or improved in a majority of children treated with a protocol adapted from migraine therapy. Further studies are required to predict those children most amenable to this approach.

127* CECOSTOMY FOR FECAL DISORDERS IN CHILDREN CLINICAL AND MANOMETRIC PREDICTIVE FACTORS. Roberto Gomez, John E. Fortunato, John Petty, Michelle Gomez-Mendez, Tom Pranikoff, Wake Forest University Baptist Medical Center, Winston Salem NC, NC

Objective: Determine clinical and manometric predictive factors for cecostomy in the treatment of constipation and fecal overflow incontinence. Methods: We performed a review of clinical and manometry data, in 32 pediatric patients (17 males, 15 females) who underwent cecostomy between 2007-2011. The mean age at time of follow-up was 9.1±4.6 years with mean follow-up time of 14.±10.9 months. Clinical outcomes were defined as: good outcome for subjects having greater than 3 bowel movements per week and less than 2 episodes of soiling per week at the time of follow up. Results: Before cecostomy the mean duration of constipation and/or fecal incontinence was 7.1±4.25 years, mean number of BMs was 1.44±0.56 per week, and soiling episodes 4.12±3.4 per week. After cecostomy 24 patients had a good outcome, and 8 had a poor outcome based on the difference in the number of weekly BM (6.96±0.20 vs. 2.6±2.1, p<0.05) and soiling episodes (0.08±0.25 vs. 1.0±2.1, p=0.073). There was no difference in the duration of symptoms between groups. There was an observed trend towards decreased number of sigmoid high amplitude propagating contractions (HAPCs) in the poor outcome group (9/24 vs 6/8) (p=0.07) and increased incidence of defecation after Bisacodyl stimulation during colonic manometry in the good outcome (11/21 vs 1/8) group. (P=0.06). There were no other differences in colonic manometry between the two groups. There was a small decrease in anorectal sensation in the poor outcome (10/17 vs 1/6) group p=0.09, but otherwise no differences in anorectal manometry (i.e., resting and squeeze pressures, RAIR, paradoxical contractions of the external sphincter, or balloon expulsion). There was no difference in the incidence of attention deficit disorder between the groups. Conclusion: Decreased motility in the sigmoid colon and anorectal sensation may be associated with poor outcome after cecostomy. Prospective studies with large sample sizes are needed to determine the prognostic factors before performing cecostomy in patient with defecation disorders.

128* EARLY PREDICTIVE FACTORS FOR THE OCCURRENCE OF COMPLICATIONS IN CHILDREN WITH TRACHEOESOPHAGEAL FISTULA. Usha Krishnan¹, Ruzanna Shah², Vincent Varjavandi³, ¹Paediatric Gastroenterology, Sydney Children's Hospital, Sydney, NSW, Australia; ²University of New South Wales, Sydney, NSW, Australia; ³Paediatric Surgery, Sydney Children's Hospital, Sydney, NSW, Australia

Introduction: Children with oesophageal atresia(OA) experience several oesophageal and respiratory complications which significantly affect their health status. These complications may include gastroesophageal reflux disease (GORD), chest infections, "cyanotic spells", early and late oesophageal strictures and need for further surgery including gastrosotomy, fundoplication and aortopexy. The objective of this study was to describe the incidence of complications in children with OA at a tertiary paediatric hospital and to identify early predictive factors for their occurrence.

Patients and methods: A retrospective chart review of 110 patients born in or transferred to Sydney children's hospital for OA repair between January 1999 and December 2010 was done. Both univariate and multivariate logistic regression analysis was done to identify early predictive factors for the occurrence of complications in these children.
Results: 100 patients were included; 55% were female; mean gestation = 36.4 weeks; mean birth weight = 2620 grams. 91% had Type C OA and 7% had long gap. Overall, 26% had associated congenital anomaly; 14% had VACTERL and 5% had the CHARGE association. None of the patients had died at the time of our study.

Conclusion: This study is the first to identify early predictive factors for the incidence of complications in children with OA. Future prospective studies are required in this area to substantiate this finding.

Table One: Incidence of complications and significant early predictive factors

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence of the complication (%)</th>
<th>Significant factors on univariate analysis: Odds ratio (95% confidence interval)</th>
<th>Significant factors on multivariate analysis (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early stricture (&lt;1 year)</td>
<td>31</td>
<td>Long gap: 16.32 (1.87-142.5)</td>
<td></td>
</tr>
<tr>
<td>Late stricture (&gt;1 year)</td>
<td>15</td>
<td>1. Long gap: 5.598 (1.635-19.17) 2. GORD: 9.939 (1.959-50.44)</td>
<td>Long gap (p= 0.007)</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>19</td>
<td>1. Long gap: 36.92 (4.103-332.3) 2. GORD: 5.727 (1.902-17.25)</td>
<td>1. Long gap (p= 0.001) 2. GORD (p= 0.002)</td>
</tr>
<tr>
<td>Cyanotic spells</td>
<td>7</td>
<td>Severe tracheomalacia: 180 (16.17-2004)</td>
<td></td>
</tr>
<tr>
<td>Chest infections</td>
<td>23</td>
<td>Early strictures: 3.330 (1.264-8.773)</td>
<td></td>
</tr>
</tbody>
</table>

129* MANAGEMENT OF PEDIATRIC PATIENTS WITH REFRACTORY CONSTIPATION WHO FAIL CECOSTOMY. Silvana Bonilla1, Alejandro Flores1, Bruce Orkin2, 1Tufts University, Boston, MA; 2Tufts University, Boston, MA

Background-Antegrade continence enema (ACE) is a recognized therapeutic option in the management of children with refractory constipation (RC). Several techniques have been reported including laparoscopic-assisted percutaneous endoscopic cecostomies (LAPEC). Data on the long-term outcome of patients that fail to improve after an ACE procedure is lacking.

Aim: To describe the rate of LAPEC failure in pediatric patients with RC, and the management and long term outcome of these patients.

Study design-Retrospective analysis of medical records of a cohort of patients that underwent LAPEC and had at least 3-year follow-up. Detailed analysis of subsequent treatment and outcome of those patients with a poor functional outcome was performed.

Results-76 patients underwent LAPEC (study period 2003-2011). 12(16%) failed successful bowel management requiring additional intervention. Mean age was 14.7±1.2 SEM (range 11-23). Mean follow-up was 66.3 months (range 35-95) after ACE procedure. All patients had RC. Colonic motility studies demonstrated colonic neuropathy in 7 patients, partially propagated-HAPCs in 4 patients, and abnormal left-sided colonic motility in 1 patient. All 12 patients were ultimately treated surgically. 6(50%) underwent laparoscopic total abdominal colectomy with ileorectal anastomosis. 2(17%) had laparoscopic colectomy with ileo-distal sigmoid anastomosis. 2(17%) underwent laparoscopic left-hemi colectomy with colorectal anastomosis (CRA). 1(8%) underwent laparoscopic subtotal colectomy with CRA, and 1(8%) had laparoscopic sigmoid resection with CRA for short-segment dysfunction. 9 patients (75%) had marked clinical improvement after surgery while 3(25%) have continued issues including fecal incontinence and ileorectal anatomic bleed.

Conclusion-In this small cohort of patients with bowel management failure after ACE-procedure, colonic resection led to improvement or resolution of symptoms in the majority of patients. However, this is a complex and heterogeneous group and some patients will have continued issues. Colonic neuropathy on motility studies is associated with poor long-term outcome.
Fellow Research Award

130 MS-275, A CLASS I SPECIFIC HISTONE DEACETYLASE INHIBITOR, IS HEPATO-PROTECTIVE IN NON-ALCOHOLIC STEATOHEPATITIS. Elizabeth L. Yu1,2, Michael Downes2, Ronald M. Evans2, 1Pediatric Gastroenterology, Hepatology and Nutrition, UCSD, La Jolla, CA; 2The Salk Institute for Biological Studies, La Jolla, CA

Background/Aims: Histone deacetylase inhibitors (HDACis) induce transcriptional activation through increased chromatin accessibility. HDACis, already in use clinically, also have anti-inflammatory activity. We hypothesize that HDACis may be hepato-protective in non-alcoholic steatohepatitis (NASH). Methods: In vitro and in vivo models were utilized. Primary hepatocytes were isolated from WT mice and treated overnight with vehicle or MS-275, a class I specific HDACi. Gene expression was examined via qRT-PCR. CDAA (choline-deficient L-amino acid defined) diet induced NASH and DIO (diet induced obesity) murine models were investigated. After CDAA diet induced steatohepatitis, mice were maintained on a CDAA diet with or without MS-275 250 mg/kg admixed in for 8 weeks. In the DIO cohort, mice were fed a high fat diet for 14 weeks then treated with 4 weeks of daily intraperitoneal MS-275 (5 mg/kg/day) or vehicle. Results: Hepatic gene expression after treatment with MS-275 demonstrated upregulation of PPARα (p<0.05), CPT-1α (p<0.05), PPARγ (p<0.05), and PGC-1α (p<0.05) and had repressive effects on pro-fibrotic factor CTGF (p<0.001). MS-275 treatment in CDAA diet fed mice resulted in significantly decreased levels of steatosis compared to untreated mice. MS-275 treatment in DIO mice also demonstrated normalization of ALT and AST, improved glucose tolerance, and lowered serum cholesterol, triglyceride (TG) and insulin after 4 weeks compared to their untreated counterparts. Histologic exam showed decreased macrovesicular steatosis and clearance of centrilobular steatosis in MS-275 treated mice on a HFD. Conclusion: MS-275 is hepato-protective in both in vitro and in vivo models. Gene expression patterns suggest that MS-275 increases beta-oxidation and oxidative phosphorylation while suppressing fibrogenesis. MS-275 treatment in murine models of NASH decreased hepatic steatosis and improved inflammatory and metabolic parameters. In conclusion, MS-275 is a promising therapeutic candidate in NASH.

Young Faculty Clinical Investigator Award

131 DIFFERENTIAL EPITHELIAL GENE EXPRESSION MAY DIFFERENTIATE EOSINOPHILIC ESOPHAGITIS (EOE) FROM GASTROESOPHAGEAL REFLUX (GER). Vincent A. Mukkada1, Andres Matoso2, Shaolei Lu2, Renee Monahan1, Kelly Cleveland2, Shamal Mangray2, Nicholas Shillingford2, Murray Resnick2, 1Pediatric Gastroenterology, Nutrition, and Liver Diseases, Hasbro Children's Hospital/Brown University, Providence, RI; 2Pathology and Laboratory Medicine, Rhode Island Hospital/Brown University, Providence, RI

Objective-To compare epithelial gene expression in patients with EoE before and after treatment to patients with GER and normal controls.

Methods-Esophageal biopsies from pediatric patients diagnosed with EoE before (EoE-BT, n=15) and a subset after successful topical steroid treatment (EoE-AT, n=6) were analyzed by gene expression microarray. Several differentially expressed epithelial genes were validated by immunohistochemistry (IHC) and RT-PCR. These were compared to normal controls (n=9) and patients with GER (n=15).

Results-Gene expression microarray identified 31 genes with greater than 3 fold change in expression compared to controls. Five of these (ALOX15, TSG6, filaggrin, SLURP1, and CRISP3) were analyzed for protein expression using IHC (Table 1). ALOX15 and TSG6 were overexpressed in EoE-BT samples, with significantly less expression in normal controls and GER patients. The EoE-AT samples showed significant decreased expression compared to matched pretreatment samples. Filaggrin, SLURP-1, and CRISP3 all had expression significantly higher in normal control and GER samples compared to EoE-BT, and significant recovery of expression of all three genes following treatment. These IHC results were then validated by RT-PCR.

Conclusion-We identified 5 epithelial genes differentially expressed in EoE, which may allow both development of diagnostic testing as well as identification of potential therapeutic targets.
### Concurrent Session I – Intestinal and Colonic Disorders

**132 SCREENING TESTS FOR CONSTIPATION IN CHILDREN: IS THE JUICE WORTH THE SQUEEZE?** Ashish Chogle, Miguel Saps, Pediatric Gastroenterology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

**Background:** Chronic constipation is a common reason for pediatric outpatient visits. NASPGHAN's guidelines recommend that the work up for chronic refractory constipation include thyroid function tests, celiac serology, calcium and lead levels. Data on the yield and financial implications of these guidelines are limited. Aims: To calculate the rate and costs of diagnosing new cases of celiac disease (CD), hypothyroidism (HT), hypercalcemia and lead toxicity in children with refractory chronic constipation following NASPGHAN guidelines' screening tests. Method: Charts of all children diagnosed with constipation (ICD-9 564) at Children's Memorial Hospital (2007-11) were reviewed. Results of thyroid function tests, celiac panel, total IgA, calcium and lead levels and costs of diagnostic investigations were analyzed. Results: 7472 children (3908 females, mean age 7.9 years) were evaluated. 1731 patients were screened for CD, 55 had elevated TTG IgA levels (>20 EIA/U) and 29 (1.7%) had CD by biopsy. 1703 patients had total IgA levels, of which 10 (0.6%) had selective IgA deficiency (<6.7 mg/dL) and only 1 (0.06%) had CD by biopsy. 2332 children had free T4 and/or TSH levels done, 14 (0.6%) were diagnosed with HT. Only 3 CD (0.17%) and 2 HT (0.08%) children had constipation as sole presenting symptom. 4651 children had calcium levels done of which 10 had high calcium (>11 mg/dL) but normal repeat values. 3 children had lead levels (all normal). Average screening cost including EGDs: $7265 per patient and $3.49 million for all patients. Cost per patient to find any abnormality (HT or CD) was $81162, finding a CD case was $120345 and finding a HT case was $249286. $224796 was spent to find an additional biopsy positive CD case in children with IgA deficiency. Over 1.3 million were spent in metabolic panels with no calcium abnormality found. Conclusion: We found a low prevalence of CD and HT among constipated children. Prevalence of CD and HT in children with constipation as the only symptom was lower than known CD and HT prevalence in general population. No calcium level abnormality was detected. Study questions the utility of blanket screening tests to evaluate children with isolated constipation.

**133 5-HT4 RECEPTORS STIMULATE ENTERIC NEURONAL DEVELOPMENT.**

Kimberley A. Chien1, Alcmeone Chalazonitis2, Zhishan Li1, Michael D. Gershon2, 1Pediatric Gastroenterology, Columbia University, New York, NY; 2Pathology and Cell Biology, Columbia University, New York, NY

5-HT is a polyfunctional GI signaling molecule and has been implicated in functional GI disorders. Because the enteric nervous system (ENS) of mice that lack neuronal tryptophan hydroxylase is hypoplastic, neuronal 5-HT is probably necessary for ENS development. Because 5-HT4 agonists stimulate enteric neurogenesis in adults, we tested the hypotheses that 5-HT4 receptors mediate serotonergic promotion of ENS development and that differentiation of neurons arising after the birth of serotonergic neurons (E8.5-15) would be 5-HT4-dependent. Effects of 5-HT4 agonists and antagonists were analyzed on development of neurons from immunoisolated enteric neural crest-derived (ENCDC) cells. Fetal mice were obtained from pregnant C57BL/6 dams at E15. ENCDC were magnetically immunoselected with antibodies to the ENCDC marker, p75NTR. ENCDC were cultured in the absence (control) or presence of a 5-HT4 agonist, RS67506, a 5-HT4 antagonist, GR113808, or both. End points included quantitation of immunocytochemically identified total neurons (HuC/D) and specific neuronal subtypes, calretinin.
and dopamine that develop, respectively, together with, or after serotonergic neurons. RS67506 significantly increased numbers of neurons developing from ENCDC; GR113808 blocked this response but, by itself, exerted no effect. In contrast to total neurons, no significant differences were observed between groups in numbers of either calretinin or dopamine neurons. GR113808 alone, however, significantly increased the proportion of neurons with a calretinin phenotype. These observations are consistent with the idea that serotonergic stimulation of enteric neuronal development is 5-HT4-mediated. The ability of 5-HT4 antagonism to increase expression of calretinin neurons suggests that 5-HT4 receptors may be constitutively active and enhance differentiation of still-to-be-identified late-appearing phenotype(s) at the expense of calretinin neuronal development.

134 LRH-1: STRUCTURE-BASED APPROACH TO DRUG DESIGN FOR GASTROINTESTINAL TUMORS. James Bayrer1, Rubatharshini Uthayaruban2, Elena Sablin2, Robert Fletterick2, 1Pediatrics, UCSF, San Francisco, CA; 2Biochemistry, University of California San Francisco, San Francisco, CA

Gastroenterological cancers such as sporadic and familial adenomatous polyposis-associated colorectal carcinoma and pancreatic cancer affect nearly 200,000 people in the United States each year, and worldwide hepatocellular carcinoma affects over a half million more. New research points to the nuclear receptor Liver Receptor Homolog-1 (LRH-1) as having a major role in gastroenterological tumorigenesis via interactions with the Wnt/β-catenin and other pathways, making LRH-1 an attractive target for drug discovery. LRH-1 belongs to the NR5A family of receptors and has critical roles in the embryological development of the gastrointestinal system including gut, liver, and pancreas, and later in bile acid and cholesterol homeostasis. Unlike most other nuclear hormone receptors, LRH-1 is constitutively active; its hormone is unknown.

Methods: We sought to develop and characterize specific, non-cytotoxic inhibitors of LRH-1 function for use as both potential therapeutic agents and more broadly as research tools for the study of organogenesis and tumorigenesis. We employed differential scanning fluorimetry (DSF), used to measure qualitative binding, to screen over two hundred compounds for association with the LRH-1 ligand binding domain.

Results: We discovered 9 unique compounds that interact with LRH-1 but not the closely related receptor SF-1. We have further demonstrated that four of these compounds have antiproliferative effects in two distinct cancer cell lines expressing LRH-1 with IC50 values ranging from 8.6 to 30 μM.

Conclusions: General features for binding shared between all compounds include a linear array of hydrophobic groups with polar atoms likely allowing for registration within the hormone pocket. Interestingly, two compounds showing antiproliferative activity share a cholesterol motif which may be related to LRH-1’s function in bile acid and cholesterol homeostasis.

Support: F32 CA163092-01A1, T32 DK007762

135 THE EFFECTS OF AMOXICILLIN AND CLAVULANIC ACID ON THE SPONTANEOUS MECHANICAL ACTIVITY OF JUVENILE RAT DUODENUM. Steven L. Ciciora, Cheryl E. Gariepy, Kent C. Williams, Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital, Columbus, OH

There are a limited number of treatments for pediatric dysmotility. Amoxicillin/clavulanic acid induces phase III contractions in the pediatric duodenum and is used off-label for dysmotility. We aim to determine how amoxicillin and clavulanic acid individually influence the spontaneous mechanical activity of rat duodenum and in turn gain an understanding of how best to use amoxicillin/clavulanic acid in children with dysmotility.

Methods: 1cm duodenal segments from juvenile rats were attached longitudinally to a force transducer in an organ bath with oxygenated Krebs buffer. The samples were equilibrated and were cumulatively exposed to either amoxicillin or clavulanic acid (0.1-100μM). The same experiments were later done in the presence of tetrodotoxin, atropine, and L-NNA. Separate samples were exposed to carbachol (0.01M) alone to assess maximal response. Samples were re-equilibrated, exposed to amoxicillin or clavulanic acid, and then re-exposed to carbachol (0.01M). Data were analyzed with ANOVA & paired t-tests.

Results: The addition of amoxicillin caused a statistically significant increase in the amplitude of the spontaneous activity at 3-100μM. Data delineating the nature of the effect of amoxicillin will be presented. Clavulanic acid did not affect the amplitude at any concentration. Neither drug affected the basal tone or the frequency of contractions. When compared to carbachol alone, stimulation with carbachol in the presence of amoxicillin (30-100μM) caused a statistically significant increase in the maximum activity.

Conclusions: The spontaneous mechanical activity of juvenile rat duodenum is increased by the presence of amoxicillin. The presence of clavulanic acid has no effect. Additionally, amoxicillin increases the maximum activity when carbachol is used to stimulate samples. This suggests that amoxicillin directly or indirectly modulates the spontaneous mechanical activity of rat duodenum. Our work begins to provide a better pharmacologic understanding for its use in patients with dysmotility.
136 MicroRNAs Are Altered in Eosinophilic Esophagitis. Calies Menard-Katcher, Alain Benitez, Nicholas J. Hand, Adam M. Zahn, Mei-Lun Wang, Joshua Friedman, Pediatrics, Division of Gastroenterology and Nutrition, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Objectives/Background: MicroRNAs (miRNAs) are small non-coding RNA molecules involved in post-transcriptional gene regulation. EoE is a chronic allergen-mediated disorder of the esophagus characterized by symptoms of esophageal dysfunction and eosinophilic infiltration of the esophageal epithelium. Several pathogenic pathways have been described in EoE, the majority of which relate to Th2 cell-mediated activation of epithelial cell inflammatory signals, eosinophilic infiltration of the esophagus and epithelial damage. In light of the widespread function of miRNA, we hypothesize that miRNA expression is altered in EoE and contributes to disease pathogenesis.

Patients and Methods: Esophageal biopsies were collected from pediatric subjects at time of upper endoscopy. RNA was isolated from 6 subjects with EoE (≥20 eos/hpf, endoscopic appearance consistent with EoE, and upper GI symptoms) and 6 matched controls. The miRNA expression profile of each sample was assessed using a direct hybridization platform. The Significance Analysis of Microarrays was used to detect differences in gene expression based on criteria of false discovery rate <10% and absolute fold change of >1.5. Alterations in miRNA levels were validated by direct quantitative PCR and validated in a larger cohort. EoE associated miRNA were also measured in subjects with active EoE, treated EoE and reflux esophagitis.

Results: Twelve miRNAs were identified to be up-regulated (eg. miR-223 and miR-21) and 2 miRNA were down-regulated (miR-375 and miR-203) in EoE compared to controls. The results of the large-scale platform were confirmed by qPCR. Select candidate EoE-associated miRNA normalized with EoE treatment and were not altered in reflux esophagitis. Using bioinformatics, multiple potential gene targets of these miRNA were indentified.

Conclusions: MiRNA are altered in EoE. These EoE-associated miRNA are likely to be involved in disease regulation or pathogenesis.

137 Esophageal Epithelial and Mesenchymal Cross-Talk Leads to Features of Epithelial to Mesenchymal Transition in Vitro. Amanda Muir, Diana Lim, Mei-Lun Wang, Children's Hospital of Philadelphia, Philadelphia, PA

Background: Esophageal fibrosis is the most serious complication of eosinophilic esophagitis (EoE). In addition to subepithelial fibrosis, epithelial to mesenchymal transition (EMT), the process by which epithelial cells acquire features of activated myofibroblasts, has been described in EoE. It is believed that activation by cytokines including TGF-β, TNF-α, and IL-1β, stimulates fibroblasts to acquire the activated phenotype of myofibroblasts. In EoE, it has been suggested that mast cells and eosinophils may be the sources of these pro-fibrogenic cytokines. To date, the role of esophageal epithelial cells as effector cells in EoE-associated tissue remodeling has never been studied. In this study, we investigated the consequences of cross-talk between esophageal epithelial cells and esophageal fibroblasts, and explored the ability of esophageal epithelial cells to develop features of EMT in vitro.

Methods/Results: We stimulated primary fetal esophageal fibroblasts (F3F) with conditioned epithelial media (CEM) from non-transformed immortalized esophageal epithelial cells (EPC2-hTERT), and found that CEM primed F3F cells to secrete IL-1β and TNF-α, but not TGF-β. To determine whether these fibroblast-derived cytokines might induce EMT, we cultured F3F cells in CEM, then transferred this fibroblast-conditioned media (FCM) onto EPC2-hTERT cells. FCM stimulation of EPC2-hTERT cells enhanced epithelial expression of α-smooth muscle actin (SMA) and decreased expression of e-cadherin by RT-PCR and immunofluorescence. To study these interactions in a physiologic model, primary EoE esophageal epithelial cells (EPC394) were stratified on a feeder layer of F3F cells in organotypic culture. In this context, EPC394 cells exhibited loss of e-cadherin and gain of SMA expression compared to control EPC2-hTERT cells. Conclusions: Our results suggest that fibrosis can occur in the absence of circulating immune effector cells, and that EMT may occur in the absence of TGF-β in vitro. Our findings suggest a critical role for esophageal epithelial cells as effector cells in EoE-associated tissue remodeling.

Abstracts   JPGN Volume 55, Suppl 1, October 2012
138 CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF NON-HELICOBACTER PYLORI (HP) GASTRITIS COMPARED TO HP GASTRITIS IN CHILDREN. Warapan Nakayuenyongsuk1,2, Ali Saad3,1, Christopher Swearengen1,2, George J. Fuchs1,2, 1Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR; 2Arkansas Children's Hospital, Little Rock, AR; 3Pathology, University of Arkansas for Medical Sciences, Little Rock, AR

Objective: With the efficacy of the eradication of Helicobacter pylori (Hp) infection, the number of children with Hp gastritis (Hp+) has significantly decreased. As a result, many children now have a disproportionately greater non-Hp type of gastritis which is poorly defined. Our study intends to investigate aspects of the epidemiology and clinical characteristics of non-Hp gastritis compared to Hp+ gastritis in our population of children.

Method: This is retrospective case-control study. Pathology records from the period 1990 to 2010 at Arkansas Children's Hospital (ACH) were searched for children age 2-20 years with chronic gastritis with and without H. pylori infection. Demographic and clinical data were abstracted from medical records and pathology reports. Histologic sections were reviewed again by one of the authors to confirm the diagnosis.

Result: Thirty Hp+ children who met our inclusion criteria and an equal number of age- and gender-matched Hp-negative (Hp-) children were identified. Among potential risk factors examined, there were no statistically significant differences between the groups in demography, housing location, medical history, presenting signs and symptoms, or a family history of peptic ulcer diseases or gastritis. Smoking in the household and Medicaid in contrast to private insurance had marginal associations. Review of the clinical presentation variables revealed a statistically significant association of reported and/or documented gastrointestinal blood loss with Hp+ gastritis.

Conclusion: In our population of children Hp+ gastritis but not Hp- gastritis was associated with gastrointestinal blood loss. No significant associations or differences were observed in demographic variables or other of the established Hp risk factors examined.

139 CLINICAL ASSOCIATIONS IN EOSINOPHILIC ESOPHAGITIS (EOE) AT TEXAS CHILDREN'S HOSPITAL EOSINOPHILIC GASTROINTESTINAL DISORDERS (EGID) CLINIC

Anthony P. Olive1, Emily R. Samuels2, Carla M. Davis3, 1Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine/Texas Children's Hospital, Houston, TX; 2Food and Nutrition Services, Texas Children's Hospital, Houston, TX; 3Pediatric Allergy and Immunology, Baylor College of Medicine/Texas Children's Hospital, Houston, TX

Background: The rapid rise in the incidence of EoE has resulted in the formation of multidisciplinary clinics to meet the unique needs of this patient population. The EGID Clinic at Texas Children's Hospital and Baylor College of Medicine began in June 2010. We report clinical associations in our patient population over the first 2 years.

Methods: Questionnaires were administered to new patients to assess current symptoms, associated atopic conditions and family history of gastrointestinal and atopic disease. The number of eosinophils (eos/hpf) on biopsy before and after treatment through the Clinic were compared. Chi-squared, Fisher's exact test and ANOVA were performed.

Results: Of 55 patients seen in the Clinic, 39 had EoE. Vomiting was a presenting complaint in 9 of 16 (56%) EoE patients with eczema, 4 of 23 (17%) without eczema (p=.017), and 2 of 16 (13%) patients older than 12 years of age, compared to 11 of 23 (48%) twelve years or younger (p=.037). Food aversion was a complaint in 5 of 16 (31%) patients with eczema and in only 1 of 23 (4%) without eczema (p=.033). Prior testing for food allergies was reported in 20 of 23 (87%) patients with a family history of asthma, compared to 6 of 16 (38%) without a family history (p=.002). Prior food reactions was reported in 15 of 23 (65%) patients with a family history of asthma, compared to 5 of 16 (31%) without a family history (p=.037). Mean eos/hpf was 61.7 at presentation compared to 11.0 after therapy received in the Clinic (p<.01).

Conclusion: In our EoE population, vomiting is associated with eczema and younger age, and food aversion with eczema. Family history of asthma is associated with likelihood of food allergy testing and food reactions. This multidisciplinary approach at TCH, comprised of a pediatric dietician, allergist, and gastroenterologist, has an impact on esophageal eosinophilia.

140 FOLLOW UP SURVEY OF THE CLASS OF 2007. WHERE ARE THEY NOW? Cary M. Qualia1, Myriah Zeien Tarantelli1, Constance D. Baldwin2, 1Pediatrics, Albany Medical Center, Albany, NY; 2Pediatrics, University of Rochester Medical Center, Rochester, NY

Objectives: Pediatric gastroenterologists are expected to acquire skills as clinicians, researchers, and educators during their fellowship training. An e-mail survey was conducted in 2010 to determine how well training experiences prepared graduates for their roles as attending physicians. Methods: A follow up survey was e-mailed to the 50 pediatric gastroenterologists who had responded to a previous survey conducted in 2006, the results of which were published in JPGN 47:327-22, 2008. Results: Surveys were completed by 35 physicians. Of these, 24 (68.5%) spend at least 75% of their time in the clinical arena. Only 9 of 35 respondents (26%) spend > 25% of their time conducting clinical and/or basic science research. 18 respondents (51%) are not currently involved in any type of research activity. Of the 24 respondents who spent over half of their time in fellowship conducting research, only 8
EARLY LIFE RISK FACTORS IN EOSINOPHILIC ESOPHAGITIS.

Contrast material. Gastrostomy is removed 10 months after the procedure, the patient is discharge with a 6 month procedure the patient presents no symptoms, an esophagram with barium is made observing the correct pass of reprogrammed four weeks after the removal of the stent with resolution of the stenotic area. Six months after the resolution of the stenosis and granulated tissue at the place of where the stent was located. A new endoscopy is (distal 1/3 of the esophagus, with an stenosis of 1.5 cm of longitude). After 21 days, the stent is removed observing By observing no significant advance the decision of placing Polyfelx Stent on the level of the stenosis was taken improvement (in response to the pneumatic balloon treatment), with longer periods of time without solid dysphagia. A period of 4 years it was dilated by pneumatic balloon by superior endoscopy noticing a partial fundoplication surgery and a gastrostomy were performed to guarantee proper food ingestion on the re-estenosis periods. For a period of 2 years it was dilated by pneumatic balloon by superior endoscopy noticing a partial improvement (in response to the pneumatic balloon treatment), with longer periods of time without solid dysphagia. By observing no significant advance the decision of placing Polyfelx Stent on the level of the stenosis was taken (distal 1/3 of the esophagus, with an stenosis of 1.5 cm of longitude). After 21 days, the stent is removed observing resolution of the stenosis and granulated tissue at the place of where the stent was located. A new endoscopy is reprogrammed four weeks after the removal of the stent with resolution of the stenotic area. Six months after the procedure the patient presents no symptoms, an esophagram with barium is made observing the correct pass of contrast material. Gastrostomy is removed 10 months after the procedure, the patient is discharge with a 6 month interval check-ups.

141 SUCCESSFUL RESOLUTION OF REFRACTORY ESOPHAGEAL STENOSIS SECONDARY TO CAUSTIC INGESTION: 1ST PLACEMENT OF POLYFLEX® ESOPHAGEAL STENT IN MEXICAN CHILDREN. Ulises Leal Quiroga, Pediatric Gastroenterology, Christus Muguerza Sur, Monterrey N.L., Mexico

Male patient that accidentally ingests at the age of 2 years caustic soda that was kept on a beverage bottle, which causes grade III burns (Maratka classification) on the lower third of the esophagus. The patient underwent esophageal dilatation for a period of 4 years observing no improvement on a governmental hospital. We took over the case at the age of 6, GERD is diagnosed by 24hr ph probe and a new endoscopy is performed with biopsies, the findings showed an stenosis at the lower third of the esophagus with a 95% diminishment of the esophagus light with a length of the stenosis of 1.5cm that allows the passage of an endoscopic instrument of 6mm following the pneumatic dilatation, biopsies were taken of the gastric antrum where an infection caused by helicobacter pylori is diagnosed, and which was eradicated with a Quadruple therapy (Nexium-Amoxillin-Clarythromicin-Pepotobismol) for a period of 14 days and eradication was corroborated by endoscopic biopsy. In the same internment a Nissen fundoplication surgery and a gastrostomy were performed to guarantee proper food ingestion on the re-estenosis periods. For a period of 2 years it was dilated by pneumatic balloon by superior endoscopy noticing a partial improvement (in response to the pneumatic balloon treatment), with longer periods of time without solid dysphagia.

142 EARLY LIFE RISK FACTORS IN EOSINOPHILIC ESOPHAGITIS. Marcella C. Radano1, Wayne Shreffler1, Qian Yuan1, Aubrey Katz1, Stephanie Kubala1, Jude Fleming1, Corinne Keer2, 1MGH Department of Pediatrics, The Food Allergy Center at MGH, and Harvard Medical School, Massachusetts General Hospital, Boston, MA; 2Department of Pediatrics and Epidemiology, Johns Hopkins University- School of Medicine, Baltimore, MD

Objectives: Little is currently known about early life risk factors in Eosinophilic Esophagitis (EoE). The aim of this study was to investigate associations between dietary, environmental and medical exposures during infancy in young subjects with and without a diagnosis of EoE.

Patients and Methods: Twenty-five subjects with EoE and 76 controls were enrolled in this study. All participants were between the ages of 1-5 years, inclusive. Subjects and controls were carefully screened for a family history of atopic disease. Frequency matching was used for atopic status and gender to ensure uniformity between the groups. Details of birth history, early feeding history, early medical history and family history were obtained for each subject via a parent-completed questionnaire.

Results: EoE patients had a significantly higher rate of hematochezia (21.7% vs 4.1%; p=0.008), use of elemental formula (20% vs 0%; p<0.001) and reflux medications (50.0% vs 16.4%; p=0.001) than controls in the first year of life. Small differences were found in the timing of introduction of some potentially allergenic foods (egg, wheat, fish) but not with others (dairy, soy, nuts). There were no significant differences between the groups on measures of breastfeeding or timing of first solid food introduction. EoE patients were more frequently born by cesarean section than controls (62.5% vs 37.5%; p=0.021). There was also a significantly higher rate of antibiotic use in the 1st year of life (66.7% vs 32.4% p=0.003) in children with EoE.

Conclusions: This case-control study identified cesarean delivery and antibiotic use in the first year of life as strong risk factors for EoE, suggesting a role for altered microbiota in this disease. In addition, we showed that children with EoE demonstrated early signs of gastrointestinal allergy, including involvement of the lower GI tract.
143 OUTCOMES OF TRIPLE ENDOSCOPIES IN OUR PEDIATRIC VOICE, AIRWAY AND SWALLOWING CLINIC WITH EMPHASIS ON GI FINDINGS. Jyoti Ramakrishna1, Shilpa Ojha2, Daniel Sternberg3, Mary S. Fracchia2, Jean Ashland4, Christopher Hartnick4, 1Pediatrics/Pediatric GI & Nutrition, Mass General Hospital (MGH), Boston, MA; 2Pediatrics/Pediatric Pulmonary, Mass General Hospital, Boston, MA; 3Speech, Language and Swallowing Disorders, Mass General Hospital, Boston, MA; 4Pediatric Otolaryngology, Mass Eye and Ear Infirmary (MEEI), Boston, MA

Aim: To report on findings from triple endoscopies performed at the Airway Program of MGH/MEEI over the past 9 years. Background: This clinic is a unique combined venture between MGH (Ped GI, Speech Path and Ped Pulm) and MEEI (Ped ENT). To date over 2800 patients have been evaluated. Between March 2003 and February 2012, over 500 triple endoscopies (rigid laryngoscopy, flexible bronchoscopy, upper GI endoscopy) were performed. We are in the process of analysing the outcomes and have results from the first 190 patients. We will have data on the entire series shortly. Methods: Using retrospective chart review, presenting symptoms, findings from endoscopy, and final diagnosis were noted. Results: So far 190 patients have been analysed: 126 males, 64 females; age 1 month to 18 years; 73 were ≤ 2 years old, 117 were > 2 with mean age of 4.35 years. Presenting complaints include chronic cough (48%), breathing difficulties (23%) and feeding difficulties/aspiration (16%). 117/190 patients were diagnosed with GE reflux, 4/190 with eosinophilic esophagitis; the rest had laryngeal cleft, subglottic stenosis, tracheomalacia etc. We separated them by age (≤ 2 years, > 2 years old) for subgroup analysis. Discussion: We will comment on the GI outcomes of triple endoscopy with respect to final diagnosis and management in all patients in our series.

144 ADVERSE EFFECTS OF PROTON PUMP INHIBITORS IN MEXICAN CHILDREN TREATED IN A TERTIARY REFERRAL PEDIATRIC HOSPITAL. Jaime M. Ramirez, Ericka B. Montijo, Nadine M. Frank, Cervantes R. Bustamante, Jose F. Cadena, Flora Zárate, Monserrat M. Cazares, Erick M. Toro, Jorge T. Romero, Gastroenterology and Nutrition, Instituto Nacional de Pediatría, Mexico, Mexico

Background: Proton pump inhibitors (PPI) are the most effective acid suppressing drugs used in children. The most common known side effects are headache, xerostomia, dizziness, and diarrhea. Recent controversial reports have been published about adverse effects associated to prolonged use of PPIs including: gastroenteritis and gastric polyps in pediatric patients, and pneumonia, acute interstitial nefritis (AIN), bone fractures, vitamin B12, iron, calcium and magnesium deficiencies in adults. Objective: To describe the adverse effects recently reported in literature, in pediatric patients attended in Gastroenterology Department at the National Institute of Pediatrics, with prolonged PPI use, from 2009 - 2011. Methods: Retrospective review of medical records of children with PPIs use for at least 4 months, at our institution from 1/2009 to 12/2011, to determine the presence of gastroenteritis, pneumonia, acute interstitial nefritis, and bone fractures. Results: 42 patients (61.9% male, mean age 7.2 yrs) met inclusion criteria. 34/42 (81%) patients received omeprazole, 8/42 (19%) received esomeprazole. Mean age for starting treatment was 64.97 +/- 60 months, average treatment duration was 16.38 +/- 11.65 monthds. 3/42 (7.1%) patients developed pneumonia. 1/3 at 6 months of use, 1/3 at 7 months of treatment, and 1/3 developed pneumonia by influenza H1N1 at 9 months of therapy. There were no reports of gastroenteritis, bone fractures, acute interstitial nephritis, or clinical symptoms of iron or vitamin B12 anaemia. Conclusion: PPIs can be considered safe as an acid inhibitors for use in pediatric patients. There is no evidence or prospective studies of adverse effects due to prolonged PPIs use in pediatric patients, only reports of gastric polips, so a prospective study is needed to establish further evidence. 

145 INGESTION OF RADIOPAQUE AND NON-RADIOPAQUE FOREIGN BODIES: FALSE NEGATIVE MATTERS. Miguel Saps1, Silvanna Bonilla2, Jacob S. Ecanow3, 1Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2The Floating Hospital for Children at Tufts University Medical Center, Boston, MA; 3NorthShore University Health System, University of Chicago Pritzker School of Medicine, Chicago, IL

Foreign body ingestion (IFB) is common in children. Parents frequently report possible IFB that was un witnessed. Pediatric GI often order radiology (XR) but FB visibility (Vi) not always known. Not finding FB may mean no ingestion or non-Vi FB. Uncertain Vi of FB may prevent extracting dangerous FBs or lead to unnecessary interventions. Aims: Assess Vi of common FB in children. Methods: Ingestible objects selected by pediatric GI, nurses and parents. Most packages had "choking hazard" warnings. A) Body Simulation- Model with x-ray attenuation of child's body made from a water equivalent phantom (WE) with a custom prepared gelatin slab (GS) to encase FB was constructed with cracks and fissures to act as "false positives." B) Process validation: Model validated by comparing visual XR density and measured CT density to known standards. D) FB -XRs of 14 FB (12 items + 2 copies) encased in models of different thickness to determine visibility in children of different sizes. XRs performed with various techniques to account for practice variations. E) Vi - 5 board certified radiologists (RD)
Abstracts

(>10 year experience) blinded to number and identity items shown in XR simulating 20 cm thick child asked to number visible items and identify item shape. Results: 5 RDs described: 8,8,7,8,9 objects; false positives: 1,1,1,2,2. True Positive: 7,7,6,6,7. Sensitivity: 58,58,50,50,58%. High agreement objects seen/not seen. 5 RD found same 6 FB. 4 other FBs never seen. Conclusion: Total agreement in some objects, others never seen in XR (possibly missed in practice). Unknown Vi could lead to child mismanagement. Registry of visibility is advised.

146 GASTROINTESTINAL MANIFESTATIONS OF THE 22Q11.2 DELETION SYNDROME

Objectives: The 22q11.2 deletion syndrome (22q11.2DS) and its association with GI manifestations have been previously described (Mascarenhas et al., 2010) from within a large database of patients being followed at CHOP. These manifestations were characterized using exploratory data analysis.

Methods: Medical records of 857 individuals with 22q11.2DS enrolled in an ongoing IRB-approved research study were retrospectively reviewed. Probability distributions and regression analyses were used.

Results: Within the large database (n = 857), the age-wise distribution was largely non-parametric (mean = 5.07 yrs, SD = 6.93 mo). A regression analysis of the effect of age, ethnicity and gender did not reveal a significant effect of any of these factors (P ≥ 0.05). Key symptoms (feeding problems, reflux, constipation, vomiting, and swallowing problems) were used to derive a composite GI symptom score (no symptoms = 0; all 5 symptoms = 5). An additional regression analysis showed a positive relationship between age and this composite score (R2 = 0.016, P < 0.05). Using a cumulative probability function, we show that ≥90% of patients presented with a score of ≤2. Subsequently, we used a subset of patients to determine the likelihood of an abnormal diagnostic test. UGI series, MBS, milk scan, EGD and biopsy were included in this analysis. Using a binomial probability function, the likelihood of any one abnormal diagnostic test was ≤10%.

Conclusions. In this series, the GI manifestations of 22q11.2 deletion syndrome are described in detail. As shown here, patients are likely to present with one symptom alone, and further testing may not accurately predict presence of significant GI pathology, often complicating diagnosis. These results support prompt referral to a specialized GI center as early as possible to avoid delays in diagnosis.

147 DUAL CHANNEL COMBINED INTRAGASTRIC (IG) AND INTRAESOPHAGEAL (IE) PH EVALUATIONS IN PREMATURE INFANTS TREATED WITH RABEPRAZOLE FOR GASTROESOPHAGEAL REFLUX DISEASE.
William Treem1, Wanda Furmaga-Jablonska2, Antoni D’Souza3, Bhavna Solanki1, Beata Wiackiewicz1, Dianne Hoffman1, An Thyssen1, 1Janssen Research and Development, LLC, Titusville, NJ; 2Dzieciecy Szpital Kliniczny im Prof A Gebali, Lublin, Poland; 3SUNY Downstate Medical Center, Brooklyn, NY

Background and aims: The pharmacokinetics (PK) and pharmacodynamics (PD) of rabeprazole have not been studied in premature neonates with gastroesophageal reflux disease (GERD).

Methods: A PK/PD study of rabeprazole in 69 patients <44 weeks corrected age with GERD in a Neonatal Intensive Care Unit. Three dual IG/IE pH studies were done at baseline (day -1, prior to dosing), day 1 (single dose), and day 5 (steady-state dose) in 34 subjects. Parameters assessed included % time IG and IE pH <4.0; AUC IG and IE [H+]; and brief and prolonged (>5min) acid reflux events. Infants undergoing pH evaluation received 1 mg qd (n= 18 non-randomized), 2 mg qd or 3 mg qd (n=8 randomized to each dose).

Results: Baseline parameters were similar for all groups except for increases in % time IG pH <4.0, and the number of prolonged acid reflux events in the 3mg vs. 1mg groups; and increased baseline AUC IE [H+] in the 3 mg vs. 1 mg and 2 mg groups. All groups showed significant reductions in % time IG pH <4.0 on dosing days 1 and 5 vs. baseline. For all groups, marked reduction (90%-97%) of the AUC of IG [H+] was already present on day 1 and did not change substantially by day 5. Only the 3 mg group demonstrated significant decreases on day 5 vs. baseline in % time IE pH <4.0 and AUC IE [H+], and in the number of prolonged acid reflux events.

Conclusions: One mg rabeprazole suppressed gastric acid on the first day of dosing and a 2-3 fold increased dose did not appreciably change the overall IG [H+]. Three mg rabeprazole reduced IE exposure to H+ and reflux events in infants with more severe acid reflux at baseline. Future PK analysis will correlate plasma drug exposure with effects on the IG and IE acid milieu.
148 NORMAL AND PPI-MEDIATED GASTRIN LEVELS IN INFANTS 1-11 MONTHS OF AGE.

William Treem1, Sunny Hussain2, Jaroslav Kierkus3, Peter Hu1, Dianne Hoffman1, Ray Lekich1, Sheldon Sloan1
1Janssen Research and Development, L.L.C, Titusville, NJ; 2WK Pediatric Gastroenterology & Research, Shreveport, LA; 3Instytut "Pomnik-Centrum Zdrowia Dziecka", Warsaw, Poland

Aim: We studied the efficacy of Rab in infants with GERD in the largest placebo-controlled trial yet conducted. Methods: Infants >44 weeks corrected age with symptomatic GERD, resistant to conservative therapy and exposure to H2-RAs and/or PPIs in 25%, were screened. After scoring >16 on a validated GERD symptom score (I-GERQ-R), 344 were enrolled in a 1-3 week open-label (OL) phase receiving Rab 10-mg/day. Weekly visits included repeat I-GERQ-R; review of a daily electronic diary (I-GERQ-DD) and Clinical Global Impression of Improvement (CGI-I). Improved CGI-I allowed randomization to placebo, Rab 5mg or 10 mg in a 5 week double-blind (DB) withdrawal phase.. Primary endpoints evaluated from baseline DB to end of DB included frequency of regurgitation; weight for age z-score; I-GERQ-R; review of a daily electronic diary (I-GERQ-DD) and Clinical Global Impression of Improvement (CGI-I).

Results: 268 patients were randomized (90 placebo; 90 Rab 5mg; 88 Rab 10mg). After equal early terminations from EOS EoE: A PRELIMINARY REPORT.

Hanh Vo1, Evan Grossman2, Virginia Anderson1, Frank Gress3, Steven M. Schwartz1, Jiliu Xu1, Adam Goodman2, Simon S. Rabinowitz1, 1Gastroenterology, Children's Hospital at Downstate, SUNY Downstate Medical Center, Brooklyn, NY; 2Gastroenterology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY; 3Pathology, Children's Hospital at Downstate, SUNY Downstate Medical Center, Brooklyn, NY

Introduction: EUS utilized to differentiate Pediatric EoE from gastroesophageal reflux (GER) and to measure response to treatment in adult EoE. This report describes preliminary EUS data in a study of the evolution of Pediatric EoE. Methods: 9 patients (6M:3F, 3-18y) with known EoE (previous esph biopsy >15 eos/hpf) had 11 EUS exams (2 studied twice) performed utilizing a 12 or 20mHz ultrasound probe at the mid-esph (n=10) and distal-esph (n=11) prior to obtaining esph biopsies during endoscopy.
Results: 3 EoE patients in remission (EoE-R; eos<15/hpf in both biopsies) had 4 EUS. One additional child had >15 eos/hpf only in distal-esph biopsy. The mean total wall thickness (TWT) obtained in these 5 EoE-R exams was mid-esph = 1.6 +/- 0.4mm (range 1.1 - 1.9mm) and distal-esph also 1.6 +/-0.4mm (range 1.1 - 2mm). This cohort had 3 children 3 years of age, with multiple food allergies who had been treated since infancy with restriction diets, acid suppression, and no oral or topical steroids. 5 other patients had active disease (EoE-A; >15 eos/hpf in both mid and distal-esph). In 6 EUS in this group, the mean TWT in the mid-esph = 2.5 +/- 0.5mm (range 1.5 - 3.3) and in distal-esph = 2.6 +/- 0.5mm (range 1.8 - 3.3). The only 2 patients with mid-esph > distal-esph TWT each had >150 eos/hpf in their mid-esph biopsies.

Discussion: These preliminary results suggest EUS can complement mucosal biopsies in assessing the progression of EoE. In a pilot group of 3 children, stringent dietary restriction, amino acid formula, and acid suppression without corticosteroids prevented the esophageal thickening reported in Pediatric EoE. EUS should be considered in future investigations evaluating EoE therapy outcomes.

Intestinal/Colonic Disorders – Non – IBD

151 DISEASE BURDEN AND COSTS OF COW'S MILK ALLERGY (CMA) IN ARGENTINA.
Christian G. Boggio Marzet1, Francisco Follett1, Martin Bózzola1, Omar Tabacco1, María del Carmen Toca1
1Pediatric Gastroenterology, Hospital "Dr.I.Pirovano", Capital Federal, Argentina; 2Pediatric Gastroenterology, Hospital Universitario Austral, Derqui, Argentina; 3Pediatric Allergy, Hospital Británico, Capital Federal, Argentina; 4Pediatric Gastroenterology, Hospital Español, Rosario, Argentina; 5Pediatric Gastroenterology, Hospital "Prof. A.Posadas", Haedo, Argentina

BACKGROUND: CMA is an adverse reaction to proteins in cow's milk. Precise diagnosis is crucial for proper management. Our aim was to determine the symptoms and evaluated the cost of CMA in 5 private centers in Argentina.

STUDY DESIGN: Retrospective cohort study of patients diagnosed with CMA between 2007-2009.

RESULTS: 118 patients were included. Mean age was 19.45 months (SD 12.04), 61 (54%) were male. Symptoms at first visit were: blood in stools 31%, colic 26%, reflux 25%, constipation 8%, other 10%. N° events before initial diet change (pre diagnosis) were GP visits 8.34 ± 8.8, gastroenterologist visits 0.74 ± 1.1 and 1.04 ± 1.95 emergency room visits; 10.17% (5.3-17.09) required hospitalization with a mean length of stay (LOS) 3.23 SD 3.41 days. The average monthly cost per patient in this period was USD 177.31 (115.78-258.42). N° events after initial diet change (post diagnosis) were GP visits 4.25 ± 5.2, gastroenterologist visit 3.83 ± 0.35 and 0.35 ± 1.79 emergency room visits, 3.4%, (1.16-5.29) required hospitalization with a mean LOS 0.5 SD 0.7 days. The average monthly cost per patient in this period was USD 78.55 (43.83, 123.5) and including the cost of treatment with formula was USD 559.20 (444.48 - 694.88). The follow-up time including pre and post diagnosis periods was 19 months (SD 15.38) and the average total cost per patient was USD 6,032.75 (3,449.36 - 8,616.02).

CONCLUSIONS Medical visits and hospitalization were greater previous to change of diet, while afterwards 86% of the cost was due to formula.

152 IMPACT OF LIVER DISEASE ON INTESTINAL REHABILITATION IN CHILDREN WITH INTESTINAL FAILURE.
Veronica Busoni, Pablo Lobos, Rodrigo Sanchez Claria, Rosana Vagni, Fernando Frangi, Daniel DAgostino, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Intestinal failure (IF) requires multidisciplinary management focused in intestinal rehabilitation (IR) aiming enteral autonomy. Small bowel transplantation is the accepted therapy when complications of parenteral nutrition (PN) occur. 50% of children with IF have evidence of mild IF associated liver disease (IFALD) after 4-12 weeks of PN. Aim: To evaluate the effect of IFALD in the outcome of children on IR therapy.

Methods: Retrospective, descriptive analysis. The primary outcome was intestinal autonomy (sustained weaning of PN); transplantation or death were considered failure of IR. IR consisted of a multidisciplinary approach involving nutritional strategies (novel lipid emulsions in PN, escalating enteral feeds), pharmacological treatment (antimotility agents, ursodeoxicolic acid, antibiotics) and/or surgical procedures. IFALD was defined as a persistent (>2 w.) elevation of liver function tests (LFT) 1.5 times above the normal reference range.

Results: Between December 2007 and June 2011, 39 children with IF were treated at our center. Median age at admission was 0.5 y (r 0-14). The overall incidence of IFALD was 62% (25/39). 18/39 (46%) were successfully weaned from TPN (G1). In 10/39 (26%) IR failed, with 10% (4/39) transplanted and 15 % dead (6/39); and 11/39 (28%) are still under IR therapy, requiring PN (G2). An odds ratio (OR) of 9.4 was obtained for successful IR in non IFALD vs IFALD patients.

Conclusion: IFALD constitutes a significant risk factor that hinders IR success. Maximizing efforts to prevent or treat IFALD, even in initial milder presentations, can improve outcome and avoid intestinal transplantation.
Impact of IFALD on IF

<table>
<thead>
<tr>
<th></th>
<th>Non IFALD</th>
<th>IFALD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Off PN G1</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>IR failure G2</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>25</td>
</tr>
</tbody>
</table>

153 IS THERE A LINK BETWEEN COWS MILK PROTEIN ALLERGY (CMPA), AND RENAL TUBULAR ACIDOSIS (RTA). Cervantes R. Bustamante, Jaime M. Ramirez, Jose F. Cadena, Carlos C. Zapata, Flora Zárate, Victor B. Hernández, Ericka B. Montijo, Monserrat M. Cazares, Gastroenterology and Nutrition, Instituto Nacional de Pediatría, Mexico, Mexico

Renal tubular acidosis (RTA) is a syndrome characterized by hyperchloremic metabolic acidosis, in which there is tubular dysfunction for the regulation of acid-base equilibrium. The Cows Milk Protein Allergy (CMPA) is a disease with high prevalence worldwide which varies from 1-12%. Its diagnosis is clinical but there are diagnostic tests with variable sensitivity and specificity.

Methods: A prospective, cross-sectional, and observational study was carried out in 37 children with clinical suspicion of CMPA, who were treated at Gastroenterology and Nutrition Department of Instituto Nacional de Pediatría, from March 2008 to November 2009. Inclusion criteria: 1-6 months old male and female infants, not weaning, negative hydrogen test, and parent's signed consent. Exclusion criteria: malnutrition, positive serology for HIV, metabolic disorders and neurological damage. A complete medical history was done for each patient under study. Laboratory studies performed included total IgE, milk precipitins, prick test, 24 hours esophageal pH metric measurements, endoscopy and rectosigmoidoscopy. An extensively hydrolyzed formula and/or elementary diet were indicated.

Results: 37 patients (21 females and 16 males) with median age range of 3.39±1.7 were included in the study. The main clinical manifestations were digestive problems in 97.2%, renal tubular acidosis (RTA) in 32%, dermatologic in 29%, and respiratory in 27% with positive result for IgE in 8.1%, 37.8% for prick test, and 40.5% for biopsy, while a positive 24-hour esophageal pH metric measurement was found in 8.1% of the cases. Treatment with extensively hydrolyzed formula showed efficacy of 72.9%.

Weight and Height alterations

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to thrive</td>
<td>14 (37,8%)</td>
</tr>
<tr>
<td>Renal tubular Acidosis (RTA)</td>
<td>12 (32,4%)</td>
</tr>
<tr>
<td>RTA proximal</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>RTA distal</td>
<td>2 (16%)</td>
</tr>
</tbody>
</table>

154 OUTCOMES AND CHARGES OF PATIENTS WITH INTESTINAL FAILURE CARED FOR WITHIN A MULTIDISCIPLINARY INTESTINAL REHABILITATION PROGRAM. Valeria C. Cohran1,2, Jessica Zimont1, Joshua Prozialeck1,2, Rick Superina1,2, 1Ann and Robert H Lurie Children's Hospital, Chicago, IL; 2Northwestern University Feinberg School of Medicine, Chicago, IL

Introduction: Introduction: Multidisciplinary teams are taking care of infants and children with intestinal failure in the hopes of improving survival and avoiding transplantation. The purpose of this study was to examine the charges and outcomes of patients with intestinal failure.

Methods: This study was a retrospective review of all patients who received TPN for ≥ 3 months and were followed by a multidisciplinary intestinal rehabilitation program. Outcomes of survival, catheter related sepsis, serum bilirubin, rehabilitation, and associated charges were assessed.

Results: Eighty nine patients receiving TPN ≥ 3 months during the time period of Jan 2004 through Jan 2011 were analyzed. 86% of patients were tapered from TPN with the remainder of children dying or eventually requiring intestinal transplant. NEC was the primary diagnosis in 37% of the patients with gastrochisis accounting for 13.4%. Patients successfully tapered from TPN had a mean of 3 ± 0.6 (n=75) infections as compared to 10 ± 2 (n=14) (p <0.001) in those who did not. Patients with ≥ 3 central venous catheter infections were 3.6 times more likely to require intestinal transplant or die (p=0.03). There was no significant difference in charges between rehabilitated patients with different primary diagnoses. Total charges for care of rehabilitated patients as compared to those who died or underwent transplant was $1,000,000 vs. $3,000,000 (p<0.01). Patients with < 30 cm were 11 times more likely to require intestinal transplant or die (p<0.0009). Serum direct bilirubin ≥ 5 mg/dl did not predict the ultimate outcome.
Conclusions: Intestinal length and the number of catheter related infections increased the likelihood of patients requiring intestinal transplant or dying. Albeit a smaller cohort, the charges of transplant patients are significantly higher than those who ultimately achieved adaptation. Successful intestinal adaptation afforded improved survival with fewer charges in this cohort.

155 THE INTESTINAL MICROBIOME OF THE PEDIATRIC SHORT BOWEL PATIENT.
Zev Davidovics1,2, Beth A. Carter1,2, Robert J. Shulman1,2, Ruth A. Luna1,2, Emily B. Hollister1,2, James Versalovic1,2
1Baylor College of Medicine, Houston, TX; 2Texas Children's Hospital, Houston, TX

Objectives: Changes in the intestinal microbiome of patients with short bowel syndrome (SBS) are thought to significantly affect clinical outcome. The aim of the study was to characterize the fecal microbiome of the pediatric SBS subject as it compared to that of healthy children. We further sought to determine if SBS subjects with differing stool frequency and consistency have varying microbial compositions.

Methods: We analyzed the bacterial composition of 21 fecal specimens from 9 children with SBS and 9 healthy children ages 9 months - 8 years by 16S ribosomal RNA gene sequencing. The sequences were quality filtered and analyzed using QIIME, the Ribosomal Database Project Classifier, and the randomForest supervised learning algorithm.

Results: The fecal microbiome of SBS subjects is different from healthy controls. Stool from SBS subjects had a significantly greater abundance of the bacterial classes Gammaproteobacteria and Bacilli. Stool from SBS subjects with increased stool frequency tended to have increased abundance of Lactobacillus (P=0.057) and decreased abundance of Ruminococcus.

Conclusions: This study shows that the fecal microbiome of SBS subjects is significantly different from healthy controls when analyzed by 16S metagenomics. Differences in the composition and function of gut microbiomes in children with SBS may affect bowel physiology and these findings may provide new opportunities for intestinal rehabilitation and clinical management.

156 CLOSTRIDIUM DIFFICILE INFECTION IN HOSPITALIZED CHILDREN: INCREASING TREND IN DISEASE INCIDENCE.
Abhishek Deshpande2, Chaitanya Pant1, Michael P. Anderson3, Curtis Donskey2, Thomas J. Sferra1,2, 1UH Rainbow Babies & Children's Hospital, Cleveland, OH; 2CWRU School of Medicine, Cleveland, OH; 3University of Oklahoma HSC, Oklahoma City, OK

Introduction: An increasing trend in Clostridium difficile infection (CDI) in hospitalized children from 1997 to 2006 was reported recently. It is unknown whether this trend has continued.

Objectives: To evaluate the most recent trends in CDI incidence and outcomes in hospitalized children within the United States, and to assess the association of CDI with other disease entities.

Methods: We utilized the Healthcare Cost and Utilization Project Kids' Inpatient Database for 2003, 2006, and 2009 (most recent years available). Cases <1 year of age were excluded. Incidences are expressed as cases per 10,000 discharges and mortality as deaths per 1,000 cases. Trend analysis was performed using the Cochran-Armitage test and the association between CDI and other variables of interest was assessed by univariate and multivariate regression analysis.

Results: There was a significant increasing trend in the incidence of pediatric CDI cases from 20.0 in 2003 to 31.5 in 2009 (P < 0.0001). The incidence of CDI was highest in children 1 - 5 years of age (50.6, P < 0.001). The lowest incidence was in the 16 - 20 year age group (20.2, P < 0.001). In the cohort of patients with CDI, there was no significant trend in mortality (2003, 16.7; 2009, 16.0; P = 0.568), rate of colectomy (2003, 8.0; 2009, 8.6; P = 0.757), or median length of hospital stay (2003, 6 days; 2009, 6 days; P = 0.771). There was an increasing trend in median hospitalization charges (2003, $23,200; 2009, $32,653; P < 0.001). CDI was present frequently in cases with hematopoietic stem cell transplant (5.1%), inflammatory bowel disease (2.5%), cancer (2.0%), fungal infections (2.0%), and human immunodeficiency virus (2.0%).

Conclusions: There is an increasing trend in CDI among hospitalized children for the most recent years available for this study (2003 - 2009). CDI does not appear to have increased in severity based upon outcome measures of colectomy, length of stay, and mortality.

157 RAPID CESSATION OF ACUTE DIARRHEA IN PEDIATRIC PATIENTS USING A NOVEL PLANT EXTRACT: RESULTS OF A RANDOMIZED, CROSS-OVER STUDY.
Arthur Dover1, K. T. Park2, Telam Noguera1, 1Dover Travel Clinic, Aptos, CA; 2Stanford University / Lucile Packard Children's Hospital, Palo Alto, CA; 3Universidad Centroamerica de Ciencias Empresariales, Managua, Nicaragua

Supportive care with oral rehydration solution (ORS) is standard treatment for acute diarrhea, although the duration of illness typically is not shortened. The objective of this study was to assess the effectiveness of a novel plant extract (LifeDrops, LiveLeaf Bioscience, San Carlos, CA) to restore bowel homeostasis in patients with acute diarrhea. With IRB approval, pediatric patients who presented to a community clinic in Nicaragua with uncontrolled diarrhea within a 48 illness period were enrolled after obtaining parental consent. Patients were randomized to either receive ORS containing the extract on day 1 and then ORS alone on day 2 (study arm) or receive ORS alone on day
1 and then ORS plus the extract on day 2 (control arm). Patients were observed under standard of care for 24 hours after consumption of the fluids and the time and number of bowel movements noted. Stool in each bowel movement were ranked using the Bristol Stool Scale (BSS). A total of 61 patients were enrolled (30 in the study arm, 31 in the control arm). Within 24 hours after intervention, patients in the study arm reported BSS stool 4 or less in a mean time of 3.1 hours versus a mean time of 9.2 hours in the control arm (p=0.002); 66% of patients in the study arm had a BSS ranking of 4 or less with the first bowel movement after drinking the ORS+extract fluid. During the second study day, patients given the ORS+extract on day 1 and then ORS alone on day 2 continued to have BSS stool 4 or less while patients that crossed over on day 2 achieved a BSS of 4 within 24 hours of consumption of the extract. For patients in the control arm, the mean number of bowel movements on day 1 (receiving ORS alone) was 4 but only 2 after receiving the extract on day 2 (p=0.0001). No adverse events were observed during the study.

Conclusion: Decreased stool frequency and a normalization of stool consistency were observed with the administration of ORS containing LifeDrops than with ORS alone.

158 PEG 3350 FOR COLON PREPARATION FOR COLONOSCOPY IN CHILDREN: A HEAD TO HEAD COMPARISON BETWEEN 2 DAYS AND 4 DAYS PROTOCOLS. Rotem Elitsur, Lisa Butcher, Vicki Lund, Yoram Elitsur, Pediatrics, Marshall University, Huntington, WV

Preparation of the colon for colonoscopy in children is a difficult task due to a poor compliance. We previously reported an adequate colon preparation (rate >92%) using PEG-3350 for 4 days (Safder 2008). In a recent publication, 2 days protocol achieved comparable results (Phatak 2011). Aim: To compared between 4 vs. 2 days colon preparation protocols. Methods: in a prospective study, children were randomly assigned for either protocol. Protocol A: 4 days PEG-3350 (1.5g/Kg), and Protocol B: 2 days PEG-3350 (2.0g/Kg) with daily Bisacodyl (5mg). In both protocols, the patients filled a questionnaire that included the number of stool/day, consistency of stool/day and side effect (n/v, abdominal pain). Colon preparation was graded from 1 to 5 (1- unprepared, 5- excellent) as previously described (Safder 2008). Colon grading ≥4 was defined as an adequate colon preparation. Colon cleansing was independently graded by the GI nurse and the endoscopist (YE) at the end of the procedure. Results: A total of 91 pts participated (A- 46, B- 45). No statistical difference was observed in any of the parameters (Table). Side effects (Abd. pain, V) were similar and minimal in both groups (30% vs. 26%, p=NS). An excellent agreement was achieved between the endoscopist and the GI nurse for colon grading (Pearson correlation >0.95). Conclusion: PEG-3350 cleansing protocol for 2 days is as good as 4 days protocol. Two days protocol has the advantage of being shorter thus, easier for children.

Clon protocol and results

<table>
<thead>
<tr>
<th>Protocol</th>
<th>4 days</th>
<th>2 days</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Patients.</td>
<td>39</td>
<td>38</td>
<td>0.792</td>
</tr>
<tr>
<td>Age (M± SD)</td>
<td>9.9± 4.5</td>
<td>9.9± 4.7</td>
<td>0.792</td>
</tr>
<tr>
<td>No Stools* (M± SD)</td>
<td>5.1± 2.5</td>
<td>7.8± 4.1</td>
<td>0.070</td>
</tr>
<tr>
<td>Consistency* (M±SD)</td>
<td>5.5± 0.7</td>
<td>5.5± 0.9</td>
<td>0.320</td>
</tr>
<tr>
<td>Colon Grading (M± SD)</td>
<td>3.4± 1.1</td>
<td>4.0± 1.0</td>
<td>0.435</td>
</tr>
<tr>
<td>Colon Grade ≥ 4#</td>
<td>22 (56.4%)</td>
<td>28 (73.6%)</td>
<td>0.177</td>
</tr>
</tbody>
</table>

* At last day of protocol; # Grade ≥ 4 considered adequate preparation.

159 PEUTZ-JEGHER SYNDROME IN CHILDHOOD: NEED FOR UPDATED RECOMMENDATIONS. Edward J. Hoffenberg1,2, Stephanie A. Goldstein1, 1Pediatrics-GI, University of Colorado School of Medicine, Aurora, CO; 2Childrens Hospital Colorado, Aurora, CO

Background and Aims: We reviewed our institution's experience with Peutz-Jegher syndrome in children to determine whether current recommendations on timing of screening and follow-up should be modified.

Methods: We reviewed the charts of all children with a diagnosis of Peutz-Jegher syndrome at our institution from 2000 to 2011, abstracting data on intussusception events, polyp characteristics, Sertoli cell tumors, family history, imaging and interventions.

Results: Of 14 children identified, 10 were males. Median age at first clinical evaluation was 4.5 years and family history and/or mucocutaneous pigmentation were the two most common factors stimulating screening. Median age at first screening test and at first polyp identification was 5 years for both. There were 7 intussusception events in 5 children, with median age of 10 years for first event. Two males had Sertoli cell tumors at 8 and 11 years. Polyps were identified during initial screening in 9 of 14 patients. Polyps were found in the stomach or duodenum in 5 (36%), small bowel in 5 (36%) and colon in 2 (14%) children. Large polyps were identified in 9 children at median age of 7
years.

**Conclusions:** Polyps and significant clinical consequences occur frequently in children with Peutz-Jegher syndrome less than 8 years of age. Revised guidelines should consider initial screening at age 4-5 with capsule endoscopy and upper and lower endoscopy as well as evaluation of males for Sertoli cell tumors.

Initial screening and surveillance with suggested modifications, 0-20 years

<table>
<thead>
<tr>
<th>Reference, Age (y)</th>
<th>Initial Screening</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beggs 8 18</td>
<td>Annual exam, CBC, LFT, testes exam to 12y CE, EGD, Colon Breast exam</td>
<td>. . . Initial screen: no polyps→CE q 3y; EGD/Colon at 18y Initial screen: polyps → CE/EGD/Colonoscopy q 3 yr Monthly breast exam</td>
</tr>
<tr>
<td>Van Lier 2010 10 20</td>
<td>. Hx, exam, testes exam, Hgb, CE EGD</td>
<td>. Hx, exam, testes, Hgb q1y after 10y, CE q 2-3y after 10y EGD q 2-5 yr after age 25-30</td>
</tr>
<tr>
<td>Giardiello 2006 Birth-12y 8</td>
<td>. Hx, exam, testes exam, blood EGD, small bowel series</td>
<td>. Yearly hx, exam, testes, blood; testes US q2y to 12y Initial screen normal → EGD/colon, Small bowel series q 2-3y, start at 18 y Initial screen positive→ EGD, Small bowel series q 2-3y</td>
</tr>
<tr>
<td>Suggested modifications 4-5</td>
<td>. CE/EGD/Colon; male exam for Sertoli cell tumors: testes exam, gynecomastia</td>
<td>. Initial screen no polyps→CE/.EGD/Colon q 2-3y Initial screen polyps→CE/EGD/Colon q 1-2y until no polyps, then q2-3y. Males:annual exam fro Sertoli cell tumor (testes exam, gynecomastia)</td>
</tr>
</tbody>
</table>


**160 CLINICAL APPLICATION OF CLINICAL SCORES AND LABORATORY MARKERS OF INFLAMMATION AND ACTIVATED COAGULATION IN CHILDREN WITH HENOCH-SCHÖNLEIN PURPURA.** Jeana Hong1,3, Hye Ran Yang2,3, Jeong Kee Seo3, 1Pediatrics, Kangwon National University Hospital, Chuncheon-si, Republic of Korea; 2Pediatrics, Seoul National University Bundang Hospital, Seongnam-si, Republic of Korea; 3Pediatrics, Seoul National University College of Medicine, Seoul, Republic of Korea

**Aims:** Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis of children. The diagnosis of HSP is mainly based on the clinical symptoms and signs such as skin rash, joint pain, abdominal pain and proteinuria or hematuria, which are associated with inflammation of small vessels. Activation of coagulation secondary to endothelial cell damage is considered as a typical feature in the pathogenesis of HSP. We aimed to determine any parameters which reflect disease activity in children with HSP by evaluating laboratory markers indicating inflammation and activated coagulation in compare with clinical scores.

**Methods:** From March 2004 to Feb 2011, 137 children with HSP and 62 healthy controls were included. The clinical scores of skin, joint, abdominal and kidney were recorded in acute phase and convalescent phase of the patients. Laboratory parameters including white blood cell count (WBC), absolute neutrophil count (ANC), hemoglobin, platelet count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, D-dimer and fibrin degradation products (FDP) were also collected in two phases.

**Results:** We could find significant difference in the level of WBC, ANC, ESR, CRP, fibrinogen, D-dimer and FDP between acute phase and convalescent phase. However, no significant differences were observed in the standard coagulation markers as platelet, PT and aPTT between two phases. The level of fibrinogen, D-dimer and FDP were significantly higher in acute phase than in convalescence phase and control group. Moreover, fibrinogen, D-dimer and FDP as well as WBC, ANC, ESR and CRP in acute phase significantly correlated with total clinical score. The patients with GI symptoms had significantly higher level of hemoglobin, WBC, ANC, CRP, fibrinogen, D-dimer and FDP than those without GI symptoms. The patients with kidney involvement had significantly lower level of hemoglobin and fibrinogen than those without kidney involvement.

**Conclusion:** The laboratory markers of activated coagulation as fibrinogen, D-dimer and FDP consistently reflect disease activity, especially in the patients with GI symptoms. We suggest that fibrinogen, D-dimer and FDP as well as inflammatory markers may be useful to monitor disease activity in patients with HSP.
161 MORTALITY AND INTESTINAL FAILURE IN SURGICAL NECROTIZING ENTEROCOLITIS.
John Kelleher1, Thomas Soltau1, Carroll Harmon1, Reed A. Dimmitt1,2, 1Pediatrics, University of Alabama, Birmingham, AL; 2Surgery, University of Alabama, Birmingham, AL
Background: The surgical management of necrotizing enterocolitis (NEC) continues to be controversial. The purpose of this study is to determine if primary peritoneal drainage (PPD) is associated with increased mortality or intestinal failure (IF) compared to primary laparotomy (LAP).
Methods: We reviewed the medical records of neonates undergoing any operation for NEC at Children's of Alabama from January 1, 1998 until December 31, 2009. Prenatal variables included birth weight, mode of delivery, race, gender, gestational age, Apgar scores at 1 and 5 minutes, and antenatal corticosteroid use. NEC variables included type of first operation and need for subsequent LAP following initial PPD. Mortality was defined as death before discharge and IF as being requiring parenteral nutrition after hospital discharge.
Results: Two hundred and forty patients met inclusion criteria. PPD was the initial operation in 114 patients (48%). As previously reported, the mean birth weight, median gestational age, and median 1 and 5 minute Apgar scores were significantly lower in the PPD group. PPD was associated with greater mortality than LAP (59% vs. 36%, p < 0.001). There was no difference in the composite outcome of mortality before discharge or survival with IF (63% vs. 53%, p =0.103). A greater percentage of surviving infants in the LAP group developed IF compared to PPD (26% vs. 12%, p = 0.042).
Conclusions: In this cohort, we observed significant selection bias toward small and potentially sicker infants undergoing PPD for NEC. While patients in the PPD had greater mortality, those surviving had less IF than the survivors in the LAP group. A large multi-center, stratified randomized clinical trial of PPD versus LAP for NEC may provide better insight in patient and operation selection.

162 RARE PRESENTATION OF 2 PRIMARY MALIGNANCIES IN THE SETTING OF A MISMATCH REPAIR GENE MUTATION. Sameer Lapsia1, Rebecca Abell1, Devina Prakash1, Anupama Chawla1, 1Pediatric Gastroenterology & Nutrition, Stony Brook Children's Hospital, Stony Brook, NY; 2Pediatric Hematology & Oncology, Stony Brook Children's Hospital, Stony Brook, NY
Colonic adenocarcinomas are extremely rare in the pediatric population, representing less than 1% of all neoplasms before the age of 21 and are found in only 0.3-1.5 children in a million. Case report: A 14 yo female of nonconsanguineous parents with 2 day hx of abdominal pain radiating to the back. CT scan revealed obstructing central soft tissue mass in the left kidney. A soft tissue mass was also seen in the descending colon. The patient was taken to the OR where a biopsy of the ureteral/renal mass was taken and found to be consistent with urothelial carcinoma. Colonoscopy was performed 2 days later, which revealed four polypoid lesions in the left side of the colon with the most proximal mass at the splenic flexure demonstrating a moderately differentiated adenocarcinoma. The two masses were determined to be two primary carcinomas based on pathology and staining. The patient then underwent genetic testing which revealed that she was homozygous for a PMS2 germline mutation. Discussion: Lynch syndrome or hereditary non-polyposis coli is the most common cancer predisposition syndrome in early onset colorectal cancer. Individuals with the genotype seen in our case have a unique syndrome exemplified by hematological malignancies (i.e., leukemias and lymphomas), brain cancers, small and large bowel tumors, as well as café-au-lait spots and other signs of neurofibromatosis type 1. This syndrome has been called childhood cancer syndrome. Deficiency of the DNA mismatch repair system in these neoplasms causes microsatellite instability leading to tumor formation. Urothelial carcinomas are rare and they have not been reported in patients who are carriers for biallelic MMR gene mutation carriers. Conclusion: Patients who are found to have early onset colorectal cancer should be screened for mutations in mismatch repair genes and have routine surveillance to evaluate for development of second GI and extraintestinal tumors.

163 ACQUIRED HETEROTOPIC GASTRIC MUCOSA AFTER GASTROJEJUNOSTOMY TUBE PLACEMENT CAUSING INTERMITTENT OBSTRUCTION. Sameer Lapsia1, Prakash Viswanathan1, Juan Carlos Bucobo2, Anupama Chawla1, Rupider Gill1, 1Pediatric Gastroenterology & Nutrition, Stony Brook Children's Hospital, Stony Brook, NY; 2Division of Gastroenterology and Hepatology, Stony Brook Hospital, Stony Brook, NY
Heterotopic gastric mucosa (HGM) is most commonly found along the intestinal tract, composed of ectopic gastric tissue. We report a case of an acquired HGM after gastrojejunostomy (G-J) placement causing intermittent obstruction in a pediatric patient. Case report: A previously healthy 14 year old male presented after suffering 3rd degree burns to over 40% of his body surface. He developed anoxic brain injury leading to oral-motor dysfunction, necessitating placement of a G-tube. The G-tube was endoscopically converted to a G-J tube due to feeding intolerance. No mucosal abnormality was noted. The patient had a repeat endoscopy several weeks after placement of the G-J tube for history of bilious emesis which revealed a 2.5 cm semi-pedunculated salmon-red colored polyp at the distal duodenum/proximal jejunum, partially obstructing the lumen. Bilious emesis resolved after the mass was resected. Biopsies revealed heterotopic gastric tissue with predominantly antral type gastric mucosa and occasional oxytotic cells. Discussion: HGM can be congenital or acquired. Our patient most likely represents a case of acquired
HGM, as previous UGI series, CT scan and an initial endoscopy at the time of the G-J tube placement did not reveal any evidence of a lesion. HGM signifies replacement of the native small intestinal mucosa by gastric epithelial tissue. It has been described in patients with IBD, celiac disease, intestinal cancers, and postirradiation enteritis. HGM has not been reported in pediatric patients following a G-J tube placement. In our case vomiting was most likely secondary to intermittent intussusception or obstruction caused by the mass. Conclusion: Although there are many causes of emesis after G-J tube placement, this case illustrates the importance of repeat endoscopy to evaluate for rare acquired anatomic causes like HGM, especially if contrast studies fail to yield a diagnosis.

164 EARLY CHALLENGE TEST IN INFANTS WITH PERSISTENT DIARRHEA, VOMITING AND SUSPECTED COW'S MILK PROTEIN ALLERGY. Alfredo Larrosa-Haro1,2, Adriana G. Cepeda-Vélez1

1Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatria CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

AIM: To evaluate an early exposure to cow's milk formula (CMF) in infants with suspected cow's milk allergy (CMA).

DESIGN: Open clinical trial. Twenty-five infants hospitalized due to persistent diarrhea, vomiting and acute malnutrition in whom CMA was suspected were studied. Before admission, all cases were fed with regular or lactose-free CMF. Besides the diagnosis and treatment protocol, patients were managed with an extensively hydrolyzed formula during four weeks. At this time, patients were exposed to a CMF (lactose-free), one-oz. daily for three days. Response to challenge was evaluated with an ad-hoc questionnaire.

RESULTS: Remission of symptoms and weight gain were achieved in 23/25 patients. 15/25 (60%) had a positive challenge test, 87% of them with the original symptoms (diarrhea/vomiting) and were considered as CMA. The remaining 40% did well on an infant CMF. In the CMA group, medians of weight/height z-score moved from -2.3 to -1.6 SD (p=0.05), hemoglobin from 11.1 to 11.7 g/dL (p=0.027), and albumin from 3.9 to 4.8 g/dL (p=0.001). D-xylene was 27.2 at time zero, before challenge 36.2 and 3 days after challenge 23.1mg/dL (p=0.007).

DISCUSSION: Improvement of infants with suspected CMA when managed on a cow's milk free diet was not enough to establish the diagnosis of CMA. Early challenge with CMF diminished 40 percentage points the initial clinical diagnosis of CMA. Early CMF exposure may support the diagnosis of CMA.

165 ORAL ROTAVIRUS IMMUNIZATION PROTECTS UNDERNOURISHED WEANLING MICE AGAINST INFECTION DESPITE REDUCED VACCINE SHEDDING AND MODULATED ANTIBODY RESPONSES. Sean R. Moore, Elizabeth Maier, Monica McNeal, Lee Denson, David Bernstein, Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background & Aims: International clinical trials of oral rotavirus vaccines report substantial reductions in vaccine efficacy among children in low-income vs. high-income countries. Defects in innate and adaptive immunity secondary to high rates of undernutrition may partially explain these disparities. Therefore we designed experiments to test the hypothesis that undernutrition impairs the immunogenicity of rotavirus vaccines in weanling mice.

Methods: Wild type BALB/c dams with 10-day-old suckling pups were randomized to a standard diet or an isocaloric, multideficient "regional basic diet" (RBD) that we have previously shown produces moderate malnutrition and key features of human environmental enteropathy, including villous blunting and impaired barrier function (Ueno et al. AJP 2011). We weaned pups to their dams' diet on day of life 21 and immunized RBD mice and well-nourished controls at 6 weeks of age with a live oral rotavirus (RRV) or a vehicle control. We then challenged immunized and unimmunized mice with murine rotavirus (EDIM) 4 weeks later. Stool and blood were collected after RRV and EDIM challenges to determine viral shedding and antibody responses. Results: RRV shedding in stool following immunization was decreased 2-fold in RBD mice vs. controls (15.1 ng/mL vs. 30.8 ng/mL, P<0.03), however protection against EDIM was undiminished. Following immunization, RBD mice had 2-fold higher anti-rotavirus serum IgA levels vs. immunized controls. Following EDIM challenge, unimmunized RBD mice had a 2-fold reduction in anti-rotavirus IgG vs. well-nourished controls (P=0.016); however, this was not significant after correcting for marked decreases in total IgG levels in RBD mice). Conclusions: Weanling undernutrition alters host immune responses to rotavirus vaccination and infection, but does not mitigate vaccine efficacy.
166 ASSOCIATION OF CLOSTRIDIUM DIFFICILE INFECTION WITH OUTCOMES OF HOSPITALIZED SOLID ORGAN TRANSPLANT RECIPIENTS. Chaitanya Pant1, Michael P. Anderson1, Judith A. O'Connor1, Candace M. Marshall1, Abhishek Deshpande2, Thomas J. Sferra1,2, 1UH Rainbow Babies & Children's Hospital, Cleveland, OH; 2CWRU School of Medicine, Cleveland, OH; 3University of Oklahoma HSC, Oklahoma City, OK

Background: Diarrhea is a frequent complication in solid organ transplant (SOT) recipients. One of the most common infectious etiologies of diarrhea in these patients is Clostridium difficile. Our objective was to investigate the association of Clostridium difficile infection (CDI) with the outcomes of hospitalized solid-organ transplant (SOT) patients.

Methods: We extracted all adult cases with discharge diagnoses of SOT or CDI from the United States Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality 2009 database. We collected outcome variables (mortality, length of hospital stay (LOS), hospitalization charges, complications of the transplanted organ, and colectomy), demographic information, and comorbidity data for each of the cases. The data were evaluated using univariate and multiple variable regression analyses.

Results: We identified 49,198 cases with SOT of which 2.7% had CDI. Univariate comparisons of cases with SOT+CDI to those with SOT-only revealed significant differences in the evaluated outcomes including in-hospital mortality (7.4% vs 2.4%, P<0.001), LOS (median 9 days vs 4 days, P<0.001), charges (median $53,808 vs $31,488, P<0.001), organ complications (38.1% vs 33.9%, P<0.001), and colectomy (1.1% vs 0.3%, P<0.001). Using multiple variable regression analyses, in the SOT cohort (SOT-only and SOT+CDI), CDI was independently associated with greater mortality (adjusted odds ratio [aOR] 2.48, 95% CI=2.22, 2.76, P<0.001), longer LOS (difference 9.6 days, 95% CI=9.3, 9.9, P<0.001), higher charges (difference $69,647, 95% CI = $66,190, $73,104, P<0.001), more complications of the transplanted organ (aOR 1.36, 95% CI=1.28, 1.44, P<0.001), and increased need for colectomy (aOR 3.10, 95% CI=2.35, 4.08, P<0.001).

Conclusions: Our results demonstrate that CDI is associated with overall significantly worse outcomes in hospitalized patients with SOT.

167 GASTROINTESTINAL BLEEDING IN HOSPITALIZED CHILDREN IN THE UNITED STATES. Chaitanya Pant1, Michael P. Anderson1, Senthil Sankararaman1, Abhishek Deshpande2, Thomas J. Sferra1,2, 1UH Rainbow Babies & Children's Hospital, Cleveland, OH; 2CWRU School of Medicine, Cleveland, OH; 3University of Oklahoma HSC, Oklahoma City, OK; 4Louisiana State University HSC, Shreveport, LA

Background: Gastrointestinal bleeding (GIB) is one of the life-threatening problems for which children require hospital inpatient care. However, the incidence and associated mortality of GIB in the pediatric age group is not well defined.

Objective: To estimate the incidence and associated mortality of GIB in hospitalized children in the United States.

Methods: We used the U.S. Healthcare Cost and Utilization Project Kids' Inpatient Database for the year 2009. Data were weighted to generate national-level estimates. We identified cases of GIB using appropriate International Classification of Diseases, 9th revision, clinical modification codes. Cases were classified by age and site of GIB (upper, lower, and unspecified). Incidences are expressed as cases per 10,000 pediatric hospitalizations per year. Data were evaluated by Chi-square test, univariate and multiple regression analyses, and appropriate tests of significance.

Results: In the United States during 2009, there were 23,383 pediatric hospitalizations with a diagnosis of GIB. The overall incidence of GIB in children was 51.3. Children 6-10 and 11-15 years of age had the highest incidence of GIB (79.6 and 84.2, respectively, P<0.001). The overall incidence of upper, lower, and unspecified GIB was 22.2, 6.8, and 24.0, respectively. The mortality of children with any diagnosis of GIB was 2.8% compared to 0.6% for children without GIB (P<0.001). The highest overall mortality was observed in cases of lower GIB (4.0%, upper 2.0%, unspecified 3.4%, P<0.001). With adjustment for demographics, disease severity, and comorbid conditions, patients with a diagnosis of GIB had an increased risk of death (adjusted odds ratio 1.68, 95% CI, 1.53-1.84).

Conclusions: GIB in children is a commonly encountered problem and is associated with significant mortality. These results help us to better understand the epidemiology of GI bleeding in children and plan for the care of these patients.

168 HIRSCHSPRUNG'S DISEASE (HD) PRESENTING AS SIGMOID VOLVULUS (SV)

Simon S. Rabinowitz1, Jiliu Xu1, Mary Zeng1, John Amodio2, Eugene Garrow3, Steven M. Schwarz1

1Gastroenterology, Children's Hospital at Downstate, SUNY Downstate Medical Center, Bklyn, NY; 2Radiology, SUNY Downstate Medical Center, Brooklyn, NY; 3Surgery, Children's Hospital at Downstate, SUNY Downstate Medical Center, Brooklyn, NY

Background and Methods: Well-described complications of HD include enterocolitis and toxic megacolon. This report describes a case of SV in an adolescent patient with undiagnosed HD and summarizes the world literature concerning this rare complication.

Results: A 12-year-old male with chronic constipation controlled by diet and polyethylene glycol (PEG) became...
Abstracts

noncompliant and was admitted for abdominal pain, distension, emesis and constipation. Rectal irrigation and nasogastric PEG infusion were unsuccessful in achieving bowel evacuation and were followed by worsening distension and respiratory distress. Abdominal radiograph demonstrated a "coffee bean sign", consistent with SV (Fig 1). Following effective colonoscopic bowel decompression and placement of a rectal tube, a rectal biopsy showed aganglionosis consistent with HD.

Discussion: Symptoms of SV include distension, pain, and constipation. Including the present case, 24 patients with HD and SV have been reported worldwide (Table 1), comprising 16 infants/children and 8 adults (M:F = 7:1). Clinical presentations ranged from acute/fulminant to chronic (Table 2), with a reported 11% mortality. In a large series of pediatric HD, the incidence of colonic volvulus was <1% (Table 1). Conversely, HD was present in ~17% of SV cases. KUB to diagnose SV was less sensitive in children than in adults (17-30% vs. 57-90%). Pediatric barium enema was diagnostic in 61-82%. Conditions that increase SV risk include ultra-short segment HD; severe chronic constipation; elongated, mobile mesosigmoid; malrotation; cerebral palsy/mental retardation; prune belly syndrome; imperforate anus; spinal muscular atrophy; and encephalopathy.

Conclusions: 1. SV is a rare complication of HD that is difficult to diagnose in children. 2. All suspected cases of SV should be screened for HD. Table 3 presents a proposed management algorithm.

169 APPENDICEAL CARCINOID TUMOR IN A PEDIATRIC PATIENT WITH CHRONIC RECURRENT ABDOMINAL PAIN. Melissa Rose, Vesta Salehi, Thomas Ciecierega, Robbyn Sockolow Pediatrics Gastroenterology, Cornell Medical College, New York, NY

Background: Appendiceal carcinoid tumors are rare neuroendocrine neoplasms but are the most common pediatric gastrointestinal malignancy (1). In children, if symptomatic, these tumors often present as acute right lower quadrant pain mimicking appendicitis with diagnosis made incidentally after appendectomy (2, 3).

Case Report: We report on Z.G., a 10 year old female who presented with 6 months of intermittent epigastric abdominal pain. Esophagogastroduodenoscopy (EGD) revealed esophageal candida, lactase deficiency, and a small duodenal ulcer. Despite appropriate treatment, her pain persisted and she was diagnosed with functional abdominal pain. Twenty months after initial presentation, she returned with worsening periumbilical pain and CT scan revealed possible early appendicitis. She was managed conservatively as her clinical status was stable. After several recurrent pain episodes, she underwent repeat EGD with colonoscopy, both of which were normal. Elective appendectomy was performed for presumed appendiceal colic with incidental finding of a 0.3x0.2cm carcinoid tumor with intramural small vessel invasion and no serosal penetration. At a four month follow-up visit, she had complete resolution of her pain.

Conclusion: Appendiceal carcinoid tumors often present similarly to acute appendicitis but can also present more subtly with recurrent abdominal pain. Therefore, it is imperative that any patient with chronic abdominal pain, especially if right lower quadrant, be considered for evaluation of appendiceal carcinoid tumor.


170 ENHANCED INDOMETHACIN-INDUCED GUT INJURY IN FORMULA-FED RAT PUPS

Amanda Schuck1, T. Phan2, E. J. Dia2, J. M. Rhoads1, L. M. Lichtenberger2, 1Pediatric Gastroenterology, University of Texas at Houston, Houston, TX; 2Integrative Biology & Pharm, UT at Houston, Houston, TX

Background: Indomethacin (indo), a prostaglandin inhibitor, is used for medical management of patent ductus arteriosus in premature neonates. Indo can induce gastroduodenal and lower intestinal injury. Corticosteroids are used in premature infants to facilitate lung maturation. In combination, corticosteroids and indo have been linked to spontaneous intestinal perforation but the mechanism is unclear. Objective: To evaluate if environmental stress induced by maternal separation/formula feeding can lead to increased indo-induced injury. Methods: 7 day old Sprague-Dawley rats were either left with dam or separated and trained to self feed with formula for 6 days prior to indo administration. Indo (5mg/kg/day) or saline was then administered subcutaneously for 3 days prior to sacrifice. Intestinal and colonic hemoglobin were measured to evaluate intestinal injury. Intestinal bile acid, jejunal sucrase activity and serum corticosterone were measured to evaluate intestinal maturity. Results: Intestinal hemoglobin levels increased nearly 2 fold in self-fed rats that received indo compared to saline. This indo-induced increase was not seen with dam-fed rats. Self-fed indo treated rats were noted to have histologic changes reflective of mild to
Abstracts

moderate injury in the ileum. Self-fed rats compared to dam-fed rats had higher luminal intestinal bile acid levels (4018 vs 1764 micromolar), sucrase activity (2.9 vs 0.36 activity units/mg protein) and corticosterone levels (108.6 vs 52.2 ng/ml). These differences could not be explained by differences in nutritional status. **Conclusions:** Environmental stress such as maternal separation and/or formula feeding may induce changes in the intestine by stimulating corticosteroid release. Premature human neonates are presented with similar stress in the NICU and may be at similar risk of increased injury after indo. We suggest that maternal milk may have a protective role against indo-induced intestinal injury and that the injury may be multifactorial, involving stress in the neonate.

**171 EPCAM DEFICIENT MICE DEMONSTRATE INTESTINAL PERMEABILITY DEFECTS.**
Mamata Sivagnanam, James Mueller, Carla Pena, Matt Mcgeough, Hal Hoffman, Pediatrics, University of California, San Diego, San Diego, CA

Congenital tufting enteropathy (CTE) is an inherited intractable diarrhea of infancy presenting with chronic diarrhea, electrolyte imbalances, and impaired growth. We previously identified mutations in the gene for Epithelial Cell Adhesion molecule (EPCAM) in our CTE patients. Performing mRNA, western blot, and immunohistochemistry in intestinal tissue from CTE patients has shown significant decreases in protein levels and a mutant form of EPCAM. We recently reported the creation of mice expressing a mutant form of EPCAM, mimicking mutations seen in CTE patients (MUT) These mice display significant morbidity and pathology resembling congenital tufting enteropathy when compared with their wild-type (WT) littersmates. Survival of mutant mice is limited to 7 days or less. Microscopic imaging of the small intestine and colon reveals significant pathologic changes throughout the duodenum, jejunum and ileum in MUT mice.

The objective of this project is to elucidate the role of EPCAM in intestinal function using permeability studies in this in vivo model. To assess barrier function FITC-labeled dextran (60mg/100g body weight of FITC-labeled dextran) was orally gavaged into four-day old WT and MUT mice. Four hours after gavage serum was collected following decapitation. Fluorescent intensity of each sample was measured on a TECAN Genios Pro plate reader. FITC-dextran concentrations were determined from standard curves generated by serial dilutions of FITC dextran. MUT mice demonstrate significantly more (303.3 ug FITC-Dextran/mL serum) FITC-Dextran in their serum as compared with WT littersmates (47.53 ug FITC-Dextran/mL serum), suggesting increased intestinal permeability. Control (normal saline sample) showed no dextran present (0.0 ng FITC-Dextran). P-value <0.0001.

This is the first murine model mimicking changes in EPCAM seen in CTE patients. Here we identify changes in permeability of the intestine present in mice with MUT EPCAM. This provides further evidence for the important role of EpCAM in the intestine. This model will serve to further clarify mechanisms of CTE.

**172 FAMILIAL ADENOMATOUS POLYPOSIS AND THYROID CANCER: METAANALYSIS OF GENOTYPE AND PHENOTYPE.**
Voytek Slowik, Seth S. Septer, Thomas M. Attard, Pediatric Gastroenterology, Children's Mercy Hospital, Kansas City, MO

**BACKGROUND:** Familial Adenomatous Polyposis (FAP) is an autosomal dominant disorder caused by mutations in APC gene and characterized by a heightened risk of colorectal and extracolonic cancer. Extracolonic surveillance is critical but is, in general poorly defined. Genotype-phenotype correlations may be useful in defining specific subpopulations at risk. Thyroid involvement, most often papillary thyroid carcinoma (PTC), has been reported in at least 1-2%. Herein our aim was to define the specific pattern of thyroid involvement, including genotype analysis, to better focus our surveillance strategies.

**METHODS:** A PubMed search was performed. Articles were accessed and histologic, genotypic; codon-mutation or (gene) segmental involvement were recorded. A database was compiled and the mutation frequency distribution was compared to a published registry of FAP patients' APC mutations in the UMD-APC Database. (The UMD APC mutations database; Beroud C, Laboratoire de genetique Moleculaire et Chromosomique, Montpellier, France, Soussi T INSERM, Hopital Necker Enfants Malades, Paris)

**RESULTS:** Seventeen studies included the requisite data on 126 patients; most were female (F:M 15:1) and average age at presentation of thyroid malignancy was 28.63 years. Tumor histology was reported in 99 patients; PTC was the most common tumor histology (N=74). Gene mutations were reported in 71 patients. Codon 1061 mutations were significantly over-represented with 23 reported patients (32.39%), while in the UMD-APC database this mutation accounted for 5.34% of all cases. The odds ratio of thyroid cancer with codon1061 mutations was 8.97 (p<0.001). Thyroid cancer with mutations in codon 1061 presented at an average age of 26.8 years (range 20-42).

**CONCLUSIONS:** Thyroid cancer associated with FAP is more common in females and is most often PTC. Individuals with FAP harboring mutations in codon 1061 are at significantly higher risk of thyroid cancer. Further studies need to address targeted thyroid cancer surveillance in this population and are needed to better define evidence-based standards.
173 ILEOCECAL LYMPHOMA PRESENTING AS SMALL BOWEL OBSTRUCTION IN A PEDIATRIC PATIENT. David Troendle, Ashish Patel, UT Southwestern, Dallas, TX
Lymphoma rarely presents as an obstructive intestinal mass. We report a case of ileocecal Burket's lymphoma in a fourteen year old female with no significant past medical history who was admitted to Children's Medical Center Dallas after presenting with progressive abdominal pain and vomiting. Admission labs were notable for a microcytic anemia with normal platelets and white count with differential, a normal metabolic panel, and no evidence of tumor lysis. Computed tomography demonstrated a heterogeneous ileocecal mass causing a partial small bowel obstruction. Endoscopic evaluation demonstrated a large mass protruding through the ileocecal valve. Biopsies from the mass were sent for frozen section which showed an atypical lymphocytic infiltrate concerning for lymphoma. Flow cytometry and histologic evaluation subsequently confirmed the diagnosis of ileocecal Burket's lymphoma. After tumor staging, she received four rounds of high dose chemotherapy under the guidance of our Oncology department with minimal toxicity. Follow-up imaging showed resolution of the ileocecal mass. Despite her initial high grade obstruction at presentation, surgical resection of the ileocecal valve and cecum was avoided. Eight months after her last dose of chemotherapy she remains in clinical remission and symptom free. While surgical resection of ileocecal lymphoma is an option, our case demonstrates that the morbidity of an ileocecal resection can be avoided using endoscopic evaluation in conjunction with high dose chemotherapy.

174 PREVALENCE OF EOSINOPHILIA IN COLOMBIAN CHILDREN UNDER 12 YEARS OF AGE WITH TISSUE AND MIGRATORY INTESTINAL PARASITES BEHAVIOR. Carlos A. Velasco-Benitez1,2, Belinda Suarez1, Cindy Alvarez2, 1Universidad del Valle, Cali, Colombia; 2Grupo de Investigacion GASTROHNUP, Cali, Colombia
Introduction: Eosinophilia (eosinophils > 500/mm3) in children with tissue and migratory intestinal parasites (IP) behavior (Ascaris lumbricoides, Strongyloides stercoralis, Hookworm and Trichuris trichiura) has been described. Objective: To determine the prevalence of eosinophilia in Colombian children and identify possible associations. Methodology: Prevalence study in 130 schools in rural area of Cali, Colombia, with tissue and migratory IP behavior. Were considered clinical (weight, height), paraclinical (eosinophils) and socio-demographic (origin, sex) variables. Statistical analysis included estimation of the prevalence of eosinophilia in children and their corresponding 95% confidence interval (IC), the estimation of other descriptive measures of interest and association analysis by multiple logistic regression. Results: In this population of children with a mean age of 4±36 months, a prevalence of 26.9% (16 mild eosinophilia (500-999 eosinophils/mm3), 7 moderate (1000-1499 eosinophils/mm3) and 12 severe (> 1500 eosinophils/mm3)) and 51% from acute malnutrition, predominantly male and being from Cali, Colombia. Eosinophilia is also associated with IP (OR = 4.7 p = 0.01) but not with a specific IP of the degree of eosinophilia. Conclusion: Almost one third of Colombian children < 12 years of age with tissue and migratory IP behavior showed eosinophilia, not being associated with a specific IP or the degree of eosinophilia.

175 IMPROVED STOOL FOR INTESTINAL PARASITES AFTER ALBENDAZOLE IN COLOMBIAN SCHOOL CHILDREN. Carlos A. Velasco-Benitez1,2, Belinda Suarez1, Cindy Alvarez2, 1Universidad del Valle, Cali, Colombia; 2Grupo de Investigacion GASTROHNUP, Cali, Colombia
Introduction: Albendazole, benzimidazole, reduces the prevalence of intestinal parasites (IP) in school children. Objective: To describe the improved stool in Colombian school children with IP (Ascaris lumbricoides, Strongyloides stercoralis, Hookworm and Trichuris trichiura) after management with albendazole. Methodology: We included 61 schools in rural areas of Cali, Colombia, with IP who were took demographics such as age and gender and anthropometric measures such as weight and height. All received 400 mg oral single dose of Albendazole. Intentionally looked for adverse effects from the use of albendazole. Baseline and day 8, they were taken 3 serial stool for counting eggs for IP. Statistical analysis included measures of central tendency such as mean and standard desviation. Results: Mean age was 8.5±2.2 years, 36 males, 30 with ascaridosis, 15 with tricocefoisosis, 1 with hookworm, 14 with tricocefoisosis more ascaridosis, and 1 with uncinariosis more tricocefoisosis. No significant differences in age, gender, type of IP, weight and height, then on day 8 of treatment with albendazole. There was existence of IP in 9 children after management with albendazole and adverse effects occurred in 22 (in 12 abdominal pain, in 10 nausea and headache, respectively, in 8 vertigo, in 6 vomiting and in 1 rash). Conclusion: There was 85.2% improved stool for intestinal parasites at day 8 after treatment with 400 mg oral single dose of Albendazole and presence of adverse effects in 36%.

176 DIETARY GANGLIOSIDE REDUCES THE INCIDENCE AND SEVERITY OF NECROTIZING ENTEROCOLITIS (NEC) BY SUSTAINING LOCAL REGULATORY IMMUNE RESPONSES. Jiliu Xu1, Virginia Anderson2, Steven M. Schwarz2, 1Pediatric Gastroenterology, Children's Hospital at Downstate, SUNY Downstate Medical Center, Brooklyn, NY; 2Pathology, SUNY Downstate Medical Center, Brooklyn, NY
Background and Aims: NEC is a leading cause of preterm infant morbidity and mortality. Gangliosides are glycosphingolipids present in colostrum and rich in enterocyte membrane microdomains. These molecular species promote enterocyte growth and differentiation, and modulate Th1/Th2 response balance. Using an in vitro NEC
model, gangliosides have been shown to reduce bowel necrosis. However, the mechanisms responsible for observed immunomodulatory activity, as well as gangliosides/potential in vivo NEC protective role remain unknown. Accordingly, this study sought both to evaluate the effects of dietary GD3, the most predominant ganglioside in rat neonatal intestine, on the clinicopathological expression of NEC in our validated rate model, and to describe associated changes in cytokine, chemokine and FOXP3 expression.

Methods: Newborn rats were gavage-fed either formula (NEC), or formula supplemented with 15 ug/ml GD3 (GD3-NEC). Dam-fed litters served as controls (DF). NEC was induced by asphyxia and cold stress. At 96 h, all animals were killed and ileal gross and histological changes were evaluated. Relative ileal cytokine and chemokine profiles were detected using standard methods. Ileal expression of FOXP3 was assessed by immunoblot analysis.

Results: GD3 decreased the incidence, gross and histopathological severity of NEC. Ileal Th1 cytokine and chemokine production was markedly increased in the NEC group compared with GD3-NEC and DF. Th2 chemokines, tissue inhibitor of metalloproteinases 1 (TIMP-1), IL-1 receptor antagonist (IL-1ra) production and FOXP3 expression were significantly upregulated in the GD3-NEC group.

Conclusion: In a rat NEC model, these data suggest that dietary GD3 exerts an intestinal protective role by modifying local immune homeostasis in favor of Th2 cell responses, via augmented FOXP3 T regulatory cell function.

177 EFFICACY OF FECAL MICROBIOTA THERAPY FOR RECALCITRANT C DIFFICILE INFECTION - A PEDIATRIC EXPERIENCE

Ritu Walia1, Shashank Garg1, Mohit Girotra3, Arieda Giekopulli1, Yusra Rani2, Carmen Cuffari2, Joanne Lanzo1, Sudhir Dutta1,2,3,1 Pediatric Gastroenterology, the Herman and Walter Samuelson’s Children’s Hospital, Baltimore, MD; 2Pediatric Gastroenterology, Johns Hopkins, Baltimore, MD; 3Gastroenterology, Sinai, Baltimore, MD; 4Gastroenterology, University of Maryland, Baltimore, MD

Fecal microbiota therapy (FMT) has emerged as an effective treatment in adults with recurrent CDI who fail conventional antibiotic therapy. There remains a paucity of data in children treated with this novel technique. We hereby report two pediatric cases with recurrent Clostridium difficile infection (CDI) treated with FMT. Case 1: 20 month old, toddler presented with a two and half month history of diarrhea, hematochezia and poor weight gain. Past medical history was significant for chronic lung disease, gastroesophageal reflux disease, and recurrent episodes of pneumonia treated with antibiotics. Case 2: 16 and a half-year-old male presented with diarrhea and abdominal pain. The stool for C difficile toxin enzyme-immunoassay (EIA) was positive in both cases with an initial response to metronidazole. However the CDI turned out to be recacitrant in both the patients with multiple relapses despite repeated courses of antibiotics like Vancomycin, Metronidazole, nitazoxamide and triodophyllin. FMT was applied in both patients for treatment of recalcitrant CDI. Donor samples were obtained from the mother of both patients who were screened for HIV, EBV, CMV, HBV, HCV, and enteric infections. Stool suspension was prepared according to standard protocol and instilled in the right colon via colonoscope. The patients have now remained asymptomatic with resolution of diarrhea, abdominal pain and weight gain after treatment with FMT. These cases demonstrate therapeutic potential of fecal bacteriotherapy in pediatric patients with recurrent CDI.

196 IMPACT OF CONCOMITANT LOW DOSE ORAL METHOTREXATE ON INFlixIMAB DURABILITY IN PEDIATRIC CROHN’S DISEASE

Elaheh Vahabnezhad1, Marla Dubinsky2, 1Pediatric Gastroenterology, University of California, Los Angeles, Los Angeles, CA; 2Pediatric Inflammatory Disease Center, Cedar Sinai Medical Center, Los Angeles, CA

Background: Concomitant use of immunomodulators, specifically thiopurines, with infliximab (IFX) has been shown to decrease immunogenicity and optimize its long-term durability. Due to hepatosplenic T cell lymphoma, clinicians are increasingly substituting low dose oral methotrexate (MTX) for thiopurines, as in rheumatoid arthritis. It is unknown whether the combination of MTX and IFX offers any efficacy or immunogenicity advantage in IBD. Aim: To evaluate the effect of concomitant oral MTX on IFX durability as compared to IFX monotherapy in pediatric CD.

Methods: Charts of patients treated with IFX at a single Pediatric IBD Center were reviewed. Responders to induction with at least 1 year follow-up were eligible and divided into 2 groups: Group 1: IFX monotherapy and Group 2: IFX+oral MTX. Primary outcome was frequency of sustained clinical remission at 1 year. Groups were also compared for time to loss of response, frequency of recaptured responders, median IFX levels and frequency of anti-IFX antibodies (ATI).

Results: Among primary responders, 30 received IFX monotherapy (Group 1) and 43 received IFX+MTX (Group 2). Median dose of MTX was 7.5 mg/wk. Sustained durable remission was achieved in 63% of patients in Group 1 and 44% in Group 2 at year 1 (p=0.11). Median time to loss of response was similar (10.6 vs 9.6mo, p=0.52), and 4/11 (36%) in Group 1 and 16/24 (67%) in Group 2 recaptured response (p=0.09) with IFX dose and/or frequency escalation. ATIs were detectable in 40% and 44% of Groups 1 and 2. (p=0.88). Median levels of ATI and IFX were similar in both groups.
Conclusion: Our preliminary data suggests that low dose oral MTX (7.5 mg/wk) does not offer an efficacy or immunogenicity advantage to IFX. Inter-individual variation in MTX metabolism may contribute to the lack of efficacy and higher doses may be needed. Future studies investigating the role of MTX dose optimization using MTX levels to enhance IFX therapeutic response are warranted.


Background: Children with Crohn disease (CD) seen in 1995-96 were deficient in height, weight and BMI compared to control subjects and had deficits in lean body mass consistent with inflammatory cachexia. We hypothesized that therapeutic advances, especially the use of anti-TNF α agents, would lead to improved anthropometrics and body composition in a modern cohort of pediatric CD patients.

Methods: Published data for 104 CD patients seen at CHOP in 1995-96 were compared to 196 subjects from the screening visit of clinical trial NCT00364130, conducted at CHOP in 2007-10. Both groups were prevalent cohorts with comparable demographics and disease duration/severity. No patients from 1995-96 and 70 patients from 2007-10 (36%) were exposed to anti-TNF agents. Height, weight and BMI z scores for age were derived from CDC growth data and compared via unpaired t tests. Lean body and fat mass were measured by DXA scans and z scores for height and age were derived from 1001 control subjects.

Results: Weight and BMI z scores improved in the modern cohort compared to the earlier group. No difference was observed for height z scores. The modern group had deficits in lean body mass but not fat mass.

Conclusions: Despite advances in medical treatment and improving weight z scores, deficits in linear growth have persisted. Further, deficits in lean body mass with preserved fat mass in the modern cohort suggest continued cachexia and potential therapeutic shortcomings.


Anthropomorphic measures in children with CD, 1995-96 and 2007-10

<table>
<thead>
<tr>
<th>Variable</th>
<th>2007-2010 (n=196)</th>
<th>1995-1996 (n=104)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height z score</td>
<td>-0.60 ± 1.02</td>
<td>-0.74 ± 1.2</td>
<td>0.330</td>
</tr>
<tr>
<td>Weight z score</td>
<td>-0.38 ± 1.16</td>
<td>-0.66 ± 1.1</td>
<td>0.043</td>
</tr>
<tr>
<td>BMI z score</td>
<td>-0.09 ± 1.07</td>
<td>-0.35 ± 1.0</td>
<td>0.038</td>
</tr>
</tbody>
</table>

Lean body mass and fat mass in children with CD, 2007-10

<table>
<thead>
<tr>
<th>Variable</th>
<th>z score for height</th>
<th>z score for age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean body mass</td>
<td>-0.61 ± 1.02</td>
<td>-1.23 ± 1.24</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.25 ± 1.0</td>
<td>0.06 ± 1.02</td>
</tr>
</tbody>
</table>

198 THE ROLE AND ASSOCIATION OF THE NADPH COMPLEX WITH VERY EARLY-ONSET IBD. Sandeep Dhillon1, Ramzi Fattouh1, Abdul Elkadri2, Wei Xu2, Thomas Walters1,6, Conghui Guo1, David Mack1,6, Hien Huynh1,6, Shairaz Baksh2, Mark Silverberg3, Consortium Neopics6, Anne Griffiths1,6, John Brumell1,6, Scott Snapper1,6, Aleixo Muise1,6, 1Gastroenterology, Hepatology, and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 2Princess Margaret Hospital, Toronto, ON, Canada; 3Children’s Hospital of Eastern Ontario, Ottawa, ON, Canada; 4Stollery Children’s Hospital, Edmonton, ON, Canada; 5Mount Sinai Hospital, Toronto, ON, Canada; 6interNational Early Onset Pediatric IBD Cohort Study, Toronto, ON, Canada; 7Boston Children’s Hospital, Boston, MA

Background: Very early-onset inflammatory bowel disease (VEO-IBD), characterized by onset before the age of 10 years, has similar features to the colitis in chronic granulomatous disease (CGD). CGD is caused by defects in the NADPH oxidase complex, resulting in phagocytes not adequately producing reactive oxygen species (ROS). In a pilot study, our group identified a functional variant in NCF2, a gene in the NADPH complex, as being uniquely associated with VEO-IBD.

Hypothesis: NADPH oxidase gene variants contribute to VEO-IBD susceptibility because of altered oxidative burst.

Methods: 159 VEO-IBD patients and 1000 healthy controls were genotyped for 75 tag single nucleotide polymorphisms (SNPs) in the NADPH oxidase genes. In addition, 59 patients were exome sequenced for these genes to identify functional variants. We found 10 potentially functional SNPs, which were then genotyped in a
larger VEO-IBD cohort. Both studies were then replicated in a separate cohort. Neutrophils from patients with functional SNPs were studied for altered ROS production.

Results: From the tag SNP analysis, a number of variants showed strong associations with VEO-IBD. In particular, RAC2 (rs1476002) showed the strongest association with VEO-IBD (P(recessive)=7.77x10^-7). Interestingly, from the exome sequencing, analysis of patients diagnosed under the age of 6 years showed that a promoter SNP in CYBA (rs72550704) was associated with Crohn's Disease (CD) (P(dominant)=4.54x10^-5), and a functional, coding NCF2 SNP (rs35012521) was associated with ulcerative colitis (UC) (P(dominant)=6.89x10^-3). A patient, diagnosed with UC at 2 years, was identified to be compound heterozygous for two functional NCF2 SNPs (rs35012521, rs17849502); this patient's neutrophils were found to have decreased superoxide production and chemotaxis.

Discussion: Identifying NADPH oxidase variants associated with VEO-IBD suggests a role of ROS production in its pathogenesis. In addition, finding functional variants in patients helps direct personalized therapies for complicated and severe cases.

199 OBLITERATION OF ALTERNATE LIGANDS OF TNFR HALTS TUMORIGENESIS IN A MURINE MODEL OF COLITIS-ASSOCIATED CARCINOMA. Ilana Fortgang, Fengqi Chang, Harrison Martin, Department of Pediatrics, Tulane University School of Medicine, New Orleans, LA

Background: The proinflammatory cytokine, tumor necrosis factor (TNF), has been extensively studied and found to play contradictory roles in activation of the immune response and tumorigenesis. Recently we reported that in experimentally induced inflammatory colitis, absence of TNF fails to protect from inflammation and neoplastic transformation, and loss of its predominant receptor (TNFR1) increases susceptibility to invasive carcinoma (Am J Physiol Gastrointest Liver Physiol 302: G195-G206, 2012). Using the same model of murine colitis-associated carcinoma (CAC), we sought to identify the putative roles of alternative ligands of TNFR. We examined the consequences of loss of the proinflammatory cytokine lymphotxin (LT), which shares 80% homology with TNF, and the growth factor progranulin (PGRN), which avidly binds to TNFR and has been implicated in the development of breast, liver and ovarian cancer but protective from murine inflammatory arthritis. Methods: Wild-type (WT), TNF-knockout (KO), LTKO and PGRNKO mice, on C57Bl/6 background, underwent treatment to induce CAC. Weights and duration and extent of hematochezia were followed over the course of treatment. At the end animals were sacrificed and their colons removed to be evaluated grossly and scored histologically for tumor burden than other genotypes. In this regard LTKO and TNFKO were comparable to each other, both inflammation, tumor burden and invasiveness. Results: PGRNKO animals had significantly less inflammation and significantly poorer than PGRNKO. Conclusion: These findings provoke consideration of the possible interactions and interruptions of these ligands and their receptors. Moreover, these results suggest new targets or combination biologic therapies for the treatment of IBD and CAC, the most significant and promising agent(s) being PGRN/α-PGRN.

200 VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE PATIENTS HAVE UNIQUE GENETIC DETERMINANTS. Abdul Elkadri1,3, Thomas Walters1,3, Wei Xu3, Karoline Fiedler1,3, Mark Silverberg4, Anne Griffiths1,3, Scott Snapper2,3, Aleixo Muise1,3, Ilana Fortgang, Fengqi Chang, Harrison Martin, Department of Pediatrics, Tulane University School of Medicine, New Orleans, LA

Very Early Onset Inflammatory Bowel Disease (VEO-IBD) (diagnosed at age < 6) is postulated to be influenced more by genetics due to: (a) earlier age of onset (b) increased family history and (c) greater disease severity/luminal extent. Recent Genome Wide Association Studies (GWAS) have not specifically focused on VEO-IBD patients. Our aim was to investigate the relationship between the age of diagnosis and a selection of Single Nucleotide Polymorphisms (SNPs) by examining for variation in allele frequency within IBD patients with differing ages of onset, utilizing the largest cohort of VEO-IBD subjects studied to date.

Method: 228 SNPs (55 with a recognized IBD association demonstrated on GWAS; 173 from putative susceptibility pathways not noted on GWAS) were tested in 1588 Caucasian patients with known non-isolated-ileal IBD recruited from SickKids and Mount Sinai Hospitals in Toronto, Canada. Selected putative pathways included extracellular matrix integrity, keratinocyte proliferation, autophagy, interleukin receptors and pathways, NADPH oxidase/CGD pathways, TNF-alpha receptor, and calcineurin regulation. Subject's Age at Diagnosis was categorized according to the Paris Classification with an additional classifier of <6 yrs. An ordinal test of trend analysis for the Minor Allelic Frequency (MAF) across the 4 age categories was performed for each SNP.

Results: Overall, 17/228 SNPs demonstrated significant ordinal trends in MAF (8/55 previously described in GWAS; 9/173 related to a putative susceptibility pathway). GWAS associated SNPs with age variation included ATG16L1, STAT3, IL23R, MST1, ICOSLG, TNFSF18, and BSN, while susceptibility pathways with a significant
 variation in age included NOX5, TRAIP, NOS2A, RAC2, PTGER4, TLR5, and CD14. Overall, 6/17 SNPs were related to Crohn's Disease, and 11/17 to Ulcerative Colitis. Overall, 6/17 SNPs were related to Crohn's Disease, and 11/17 to Ulcerative Colitis. Conclusion: VEO-IBD is a distinct IBD subgroup with a unique genetic make-up, where 8 of the 55 GWAS susceptibility SNPs had significant age variations in MAF. These findings may lead to pathway discovery in the pathogenesis of IBD leading to novel therapies.

201 DETERMINATION OF BONE AGE IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE SHOULD BECOME PART OF ROUTINE CARE. Neera Gupta1,2, Robert Lustig2, Michael Kohn2, Eric Vittinghoff2,1 Pediatrics, Columbia University School of Medicine, New York, NY; 2Pediatrics, University of California, San Francisco, San Francisco, CA

Background: Impaired growth and delayed puberty are common in pediatric Crohn's disease (CD). Bone age (BA) is important for interpretation of statural growth. Our aims are to 1] determine the distribution of BA-Z scores, 2] identify clinical factors associated with BA-Z scores, and 3] compare anthropometric Z scores based on chronological age (CA) [CA-Z] versus BA-Z in pediatric CD.

Methods: CD patients ≤ CA 15 in females and 17 years in males were enrolled in a cross-sectional study. BA was determined with left hand/wrist x-ray. 49 patients [65% male; 84% Caucasian; mean CA 13 years] examined between 1/07 and 7/09 qualified for the study.

Results: Mean BA-Z score was -1.40 ± 1.50 (standard deviation). 41% had BA-Z score < -2.0. Mean BA-Z scores were lower in females (p=.02), Caucasians (p=.006), Tanner stage 1-3 children (p=.004), and patients with colonic disease (p=.006), past corticosteroid exposure (p=.01), current azathioprine/6-mercaptopurine treatment (p=.003), or lower height (p=.006), weight (p=.001), or BMI (p=.01) CA-Z scores. Mean growth parameter BA-Z scores differed from mean growth parameter CA-Z scores (Table).

Conclusions: Low BA occurs frequently in CD. Determination of BA should become the standard of care in pediatric CD patients, allowing clinically meaningful interpretation of growth in the context of skeletal maturation, leading to improved treatment recommendations, as growth is a dynamic marker of disease status. Prospective longitudinal studies are required to clarify determinants of BA and patterns of BA advancement in CD.

Comparison between Chronological Age and Bone Age for Interpretation of Growth

<table>
<thead>
<tr>
<th>Growth Parameter</th>
<th>Z Score Difference*</th>
<th>95% CI</th>
<th>P-Val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>0.73</td>
<td>0.45-1.01</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Weight</td>
<td>0.51</td>
<td>0.29-0.74</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BMI</td>
<td>0.23</td>
<td>0.13-0.33</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*Z Score Difference= Growth Parameter BA-Z Score Minus Growth Parameter CA-Z Score

202 RESPONSE TO ENTERAL NUTRITIONAL THERAPY VERSUS ANTI-TNF AS PEDIATRIC CROHN'S DISEASE. Dale Lee1, Monica Loruss3,4, Andrew Klink5, Kernika Gupta1, Ashley Martin1, Erin Gilroy5, Lisa Nesse6, Anthony Otley5, Anne Griffiths5, Paolo Lionetti5, Frederic Bushman5, Gary Wu5, Robert N. Baldassano6, James Lewis5, Children’s Hospital of Philadelphia, Philadelphia, PA; 2Dalhousie University, Halifax, NS, Canada; 3University of Toronto, Toronto, ON, Canada; 4Meyer Children's Hospital, Florence, Italy; 5University of Pennsylvania, Philadelphia, PA

BACKGROUND: Enteral nutritional therapy (ENT) and anti-TNF-α drugs are effective in pediatric Crohn's disease (CD). Relative efficacy for symptoms and mucosal healing is unknown. PCDAI lacks specificity for intestinal inflammation, but fecal calprotectin (FCP) correlates with endoscopic assessment. Our study compares changes in PCDAI and FCP in children with CD initiating ENT or an anti-TNF.

METHODS: PCDAI and FCP were assessed in patients at the start of ENT (n=30) or anti-TNF (n=18) then at 8 weeks. Steroid exposure was documented. Remission and response were assessed with PCDAI, and FCP thresholds of ≤50, ≤250, and ≥50% reduction. Paired and unpaired t-tests and chi2 tests were used to analyze differences within and between treatment groups.

RESULTS: The ENT and anti-TNF groups had similar demographics and initial disease characteristics except for disease duration ≤6 months (ENT 50% vs. anti-TNF 93%; p=0.001). Steroid exposure was similar in both groups (23% ENT vs. 22% anti-TNF; p=0.93). Clinical remission (PCDAI ≤10) at 8 weeks was achieved by 70% ENT and 67% anti-TNF (p=0.81). The mean decline in FCP over 8 weeks was significant in both groups (paired t-tests, p<0.05): 460 µg/g (95%CI 225-697) for ENT and 661 µg/g (95%CI 335-966) for anti-TNF (p=0.30 for ENT vs. anti-TNF). FCP ≤250 at 8 weeks was achieved by 63% ENT and 39% anti-TNF (p=0.10), and a ≥50% reduction in FCP was achieved by 67% ENT and 67% anti-TNF (p=1). Analysis restricted to children with disease duration ≤6 month produced similar results to the primary analysis.

CONCLUSION: Treatment with either ENT or anti-TNFs results in high clinical remission rates and significant reductions in FCP. Remission rates and reduction in FCP were not significantly different between groups.
203 DIVERTING ILEOSTOMY FOR THE TREATMENT OF SEVERE REFRACtORY INDETERMINATE COLITIS. Lindsey Albenberg¹, Cassandra Spengler¹, Andrew Klink¹, Peter Mattei², Robert N. Baldassano¹, Petar Mamula¹, Judith R. Kelsen¹, ¹Gastroenterology, Hepatology, and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; ²General Surgery, The Children's Hospital of Philadelphia, Philadelphia, PA

Background: Diverting ileostomy is on occasion performed at The Children's Hospital of Philadelphia in patients with indeterminate colitis (IC) refractory to medical therapy. The aim of this study was to evaluate its effect on disease course and to determine whether it provided time for a change in diagnosis prior to more definitive surgical therapy.

Methods: This was a retrospective study of patients who underwent diverting ileostomy for refractory colitis from January 2000 until April 2012. Medical records were reviewed for demographics, phenotype, therapy, weight, and hospitalizations. Exclusion criteria included diversion performed for perianal, strictureing, or fistulizing disease.

Results: There were 13 patients (8 female) of which 8 (62%) presented at 6 years of age or younger. There were 2 (15%) patients with Crohn disease (CD) and 11 (85%) patients with IC. The median time from diagnosis to diversion was 15 months. All patients had failed biologic therapy. At diversion, 11/13 (85%) patients had severe disease based on Physician's Global Assessment and 11/13 were on corticosteroids. At 12 months post-diversion (PD), 8/13 (62%) patients had quiescent disease and only one was on corticosteroids (p<0.001). A significant increase in weight Z score was seen 1 year PD as compared to 1 year prior to diversion (p<0.02). Patients were hospitalized fewer days in the 1 year PD compared to 1 year prior to diversion with a trend towards statistical significance (p<0.14). Of the 11 patients with IC, 5 (45%) had a change in diagnosis which included ulcerative colitis (3), CD(1), and IPEX (1). Five patients proceeded to colectomy, 2 underwent successful reanastomosis, and 5 remain diverted. There were no surgical complications or deaths.

Conclusions: In patients with medically refractory IC, diverting ileostomy is corticosteroid sparing. It may improve outcome and allow additional time for the definitive diagnosis to be made.

204 SINGLE-CENTER LONG-TERM OUTCOMES WITH INFLIXIMAB FOR PEDIATRIC CROHN'S DISEASE. Peter Church¹,², Thomas Walters¹,², Jack Guan², Jacqueline Vertes², Karen Frost², Aleixo Muise¹,², Anne Griffiths¹,², Department of Pediatrics, University of Toronto, Toronto, ON, Canada; ²Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children, Toronto, ON, Canada

Background/Aims: Infliximab (IFX) is effective in inducing clinical response and remission in luminal Crohn's disease (CD) in children (Hyams, 2007), but pediatric data about durability of response are limited. We reviewed the effectiveness of IFX induction and scheduled maintenance treatment in achieving short- and long-term clinical remission and normal linear growth in a single-center cohort.

Patients/Methods: From 2000 to 2011 at SickKids, Toronto, 195 children (63% male; median age 14.0 yrs, IQR 3.3) with luminal inflammatory CD (20% L1; 17% L2; 63% L3) received standard IFX 3-dose induction. Median duration of diagnosed CD at initiation was 19.9 mos (range 0.3-136.8). Responders continued scheduled maintenance treatment ± immunomodulator (IM). Records were retrospectively reviewed to extract at 6 mos and annually thereafter: physician global assessment (PGA) of continued response/remission vs. loss of response, PCDAI, linear growth, colonoscopic data and levels of IFX and antibodies (ATI). Durability of response was explored using survival analysis. The effect of maintenance regimen on secondary loss of response (LoR) was assessed by chi-square.

Results: Rates of clinical response (judged by PGA) and remission (judged by PGA and PCDAI ≤10) were respectively, 91% and 80%. Longer duration of diagnosed CD was associated with a lower rate of complete response. 20% of primary responders later stopped IFX (LoR: 56%; intolerance/complication: 30%). LoR rate was linear (6 to 8%/year) over 5 years. Within 2 years, 70% required dose escalation. In subjects with LoR, ATI were present in 85%. Concurrent IM use (104/180 responders) did not significantly alter LoR, ATI or need for dose escalation. Data for patients with growth potential (Tanner 1/2 at IFX initiation) are shown in Table.

Conclusions: These long-term data support the effectiveness of IFX in achieving durable response and improving growth in patients with luminal Crohn's disease.

<table>
<thead>
<tr>
<th>Diagnosis Initiation of Infliximab</th>
<th>1 year follow-up</th>
<th>2 year follow-up</th>
<th>3 year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median height z-score (IQR)</td>
<td>-0.4 (1.05)</td>
<td>-0.87 (1.19)</td>
<td>-0.69 (1.4)</td>
</tr>
</tbody>
</table>
1Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA; 2Pediatrics, University of Chicago, Chicago, IL; 3Office of Infectious Diseases, Centers for Disease Control, Atlanta, GA; 4Pediatrics, University of California, San Francisco, San Francisco, CA; 5Pediatrics, Texas Children's Hospital, Houston, TX; 6Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; 7Children's Center for Digestive Health Care, Atlanta, GA

Mycobacterium avium paratuberculosis (MAP) has been implicated in causing Crohn's disease (CD) and requires indeterminate colitis (IC) or non-IBD. Biopsies from 51 subjects were used to standardize assay conditions and ileo-colonoscopy for evaluation of IBD. Subjects were classified per protocol with CD, ulcerative colitis (UC), compared for detection of MAP in ileal and colonic biopsies from 178 IBD-treatment-naïve children undergoing PCR for detection in human tissue. Methods: Validated nested (N-PCR)- or real-time (RT-PCR) PCR were compared for detection of MAP in ileal and colonic biopsies from 178 IBD-treatment-naïve children undergoing ileo-colonoscopy for evaluation of IBD. Subjects were classified per protocol with CD, ulcerative colitis (UC), indeterminate colitis (IC) or non-IBD. Biopsies from 51 subjects were used to standardize assay conditions and sensitivity of N-PCR and RT-PCR. Results: Detection of MAP using RT-PCR was significantly higher (17/51) compared with N-PCR (6/51, p = 0.009). RT-PCR revealed no significant difference detecting MAP positivity in either CD (7/19) versus non-IBD (8/25, p = 0.74) or all patients with IBD (9/26, p = 0.84) versus non-IBD patients. Detection of MAP did not correlate with the biopsy site (p = 0.81). RT-PCR was more sensitive for detection of MAP than N-PCR, and was therefore used to evaluate remaining samples. Of the 178 patients, 33 (18.5%) tested positive for MAP; 9 (5.5%) with CD, 4 (2.2%) with UC/IC, and 20 (11.2%) non-IBD; ρ=0.993. Race, ethnicity, Jewish ancestry, or gender was not associated with detection of MAP in children with CD compared with controls. Conclusions: In this cohort of children with new onset CD, although MAP was detected, the frequency was not higher in subjects with CD compared with subjects who did not have CD or IBD. Funded by the NIH and The Pediatric IBD Foundation.

206 FECAL MICROBIOTA TRANSPLANT IN PATIENTS WITH RECURRENT CLOSTRIDIUM DIFFICILE INFECTION WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE. George H. Russell, Jess Kaplan, Harland S. Winter, Pediatric GI & Nutrition, MGH for Children, Boston, MA

Background/Aims: Fecal Microbiota Transplant (FMT) is a promising new therapy for the eradication of recurrent C. difficile infection (RCdI) in adults with up to 90% success. The role of FMT in treating RCdI in children is not established. We present outcomes of 6 patients with RCdI treated with FMT. Methods: All patients had at least 3 documented RCdIs by toxin ELISA or PCR detection and stopped antibiotics 36 hours before FMT. Donors (parents) were screened for sexually transmitted disease and their stools tested for known pathogens. 30-40 ml of donor stool was blended with 250 ml of normal saline and filtered with sterile gauze to decrease particulate matter. The mixture was delivered via nasogastric tube or via colonoscopy into the cecum. Inflammatory Bowel Disease (IBD) activity was evaluated by Physician's Global Assessment (PGA). Results: Of 6 patients who underwent FMT (ages 3-18 years, 3 female), 5 opted for colonoscopic delivery. 3 patients were healthy except for RCdI. 3 patients had IBD: 1 with moderately active ileocolonic Crohn's disease (CD), 1 with severely active ulcerative colitis (UC), and 1 with moderately active indeterminant colitis (IC). All non-IBD patients returned to sustained health and normal bowel habits after FMT. 2 of 3 IBD patients had sustained resolution of C. difficile infection. The UC patient had immediate resolution of all symptoms for 5 days, but despite remaining free of RCdI, re-developed severe colitis and required colectomy. The IC patient had resolution of stool C. difficile toxins at 2 weeks and 2 months post FMT, but PGA did not improve and he required immunosuppressive therapy. In the child with CD, C. difficile returned 6 weeks after FMT. There was no clinical improvement and he ultimately required immunosuppressive and surgical management. Conclusion: FMT is a promising therapy for the eradication of RCdI in otherwise healthy pediatric patients. Single dose FMT for patients with IBD may temporarily eradicate C. difficile but does not appear to result in sustained benefit for IBD.

207 THE ROLE OF INDUCIBLE NITRIC OXIDE SYNTHASE VARIANTS IN VEO-IBD. Lucas Mastropaolo1, Sandeep Dhillon1, Cornelia Thöni1,2, Chris Griffiths1, Wei Xu3, Abdul Elkadri1, Conghui Guo1, David Mack4, Hien Huynh5, Shairaz Baksh5, Thomas Walters1, Consortium Neopics6, John Brumell1, Mark Silverberg1, Scott Snapper6, Alexio Muise1, 1The Hospital for Sick Children, Toronto, ON, Canada; 2Medical University Innsbruck, Innsbruck, Austria; 3Princess Margaret Hospital, Toronto, ON, Canada; 4Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 5Stollery Children's Hospital, Edmonton, AB, Canada; 6interNational Early Onset Pediatric IBD Cohort Study, Toronto, ON, Canada; 7Mount Sinai Hospital, Toronto, ON, Canada; 8Boston Children's Hospital, Boston, MA

Background: Nitric oxide (NO) produced by inducible nitric oxide synthase (iNOS) is expressed after induction by inflammatory cytokines. Colon biopsies have revealed that patients with active IBD have higher amounts of iNOS mRNA and protein expression in the intestine, compared to healthy individuals. iNOS, encoded by NOS2A, has antibacterial effects and is responsible for tissue damage when its expression is uncontrolled. The aim of this study...
is to determine if polymorphisms in NOS2A are associated with very early-onset inflammatory bowel disease (VEO-IBD; diagnosed prior to 10 years of age) and their effect on iNOS activity.

Methods: Goldengate genotyping was used in a discovery cohort, followed by Taqman genotyping in a replication cohort. A NOS2A variant was created using site-directed mutagenesis. To investigate the function of the variant, NO production was measured via Griess assay in Henle-407 cells following transient transfection and genotyped lymphoblast cell lines under non-stimulated conditions. The expression of iNOS and nitrotyrosine was examined by immunohistochemistry in colonic biopsies of 6 patients (3 patients homozygous for the protective and risk alleles).

Results: Rs2297518 (Ser608Leu) risk allele was found to be associated with VEO-IBD, -CD, and -UC. In the combined analysis of the cohorts (337 patients with VEO-IBD and 1391 healthy controls) we found a replicated association $p$ (combined) = $3.45 \times 10^{-7}$ and OR 3.5 (95% C.I. 2.1 to 6.0). Henle-407 cells and lymphoblastoid cell lines homozygous for the rs2297518 allele produced significantly more NO than cells homozygous for the protective allele. Nitrotyrosine staining of crypt cells and leukocytic infiltrates were more intense in patients homozygous for the risk allele.

Discussion: We found an iNOS variant with a Ser608Leu substitution, located in the reductase domain, associated with VEO-IBD and increased NO production. This functional variant may be responsible for the increased tissue damage and inflammation in patients with VEO-IBD.

208 FECAL MICROBIAL TRANSPLANTATION IN PEDIATRIC ULCERATIVE COLITIS - A PILOT STUDY. Sachin S. Kunde1,2, Harold Conrad2, Deborah Cloney3, Karen Lindhout2, Ashley Strothbaum3, Erin Broene3, Jill Gibson3, Terri Crumb3, Mary Duba3, Subra Kugathasan3, 1Pediatrics, Michigan State University, Grand Rapids, MI; 2Pediatric Gastroenterology, Helen DeVos Children's Hospital and Spectrum Health, Grand Rapids, MI; 3Pediatric Gastroenterology, Emory University, Atlanta, GA

Background: Fecal microbial transplantation (FMT) has been proposed as a promising new treatment option for recurrent C. difficile colitis and ulcerative colitis (UC). Interest in FMT has largely been driven by new research into the gut microbiota. We hypothesize that FMT may restore ‘abnormal’ microbiota to ‘normal’ in UC thus induce remission in active UC. We have initiated the first phase I clinical trial for FMT in pediatric UC. We evaluated PUCAI and health-related quality of life (HRQOL) as primary and secondary outcome measures respectively.

Methods: The study was approved by Spectrum Health Institutional Review Board. This single center pilot study is enrolling ten children (ages 7-21 yrs) with mild to moderate UC. Freshly prepared stool samples from adult donor were infused via enema for five total infusions. Clinical outcome was evaluated with PUCAI score. HRQOL outcome, measured using Pediatric Quality of Life Inventory - PedsQLTM, Mapi Research Trust, France, was completed by subject and parents. Maximum possible score for HRQOL is 100 and higher score indicates better HRQOL. These scores were collected at baseline and one month after FMT. Primary endpoint was defined as decrease in PUCAI by ten points. Results: We are reporting the outcome of our first subject who completed the study. PUCAI score improved from 35 (at baseline) to 0 (one month after FMT). HRQOL score improved from 78 to 90 (physical health), from 55 to 72 (psychological health) and from 39 to 78 (parent report of patient's health).

Conclusion: Fecal microbial transplantation induced clinical remission and improved health related quality of life in a patient with active ulcerative colitis within one month. More data from this phase I study will be available in near future. Further prospective studies are needed to evaluate safety and clinical efficacy of FMT.

209 FOOD ADDITIVE EFFECT ON INTESTINAL EPITHELIAL CELLS. Grace Gathungu, Leahana M. Rowehl, Bessie Shen, Anupama Chawla. Pediatrics, Division of Pediatric Gastroenterology, Stony Brook Medical Center, Stony Brook, NY

Background: Incidence of Inflammatory Bowel Disease (IBD) comprising of Crohn’s disease and Ulcerative Colitis is on the rise. In both, the presence of antigens or microbes elicits an inflammatory response and cytokine release. Food additives are increasingly being used to enhance the quality of food products. Some evidence suggests that two common additives, Allura Red (AR) and Potassium Bromate (KBrO3) may be harmful to intestinal epithelial cells.

Objective: To determine if food additives, AR and KBrO3, are harmful to intestinal epithelial cells, induce inflammation and impair intestinal tight junctions.

Methods: Caco-2 and HT-29 cells, grown separately and co-cultured at a 3:1 ratio, were treated with varying concentrations of AR, KBrO3 or cell culture media alone. Cell proliferation was determined using alamarBlue cell viability reagent. At 24 hours, IL-6 and IL-8 levels were measured using ELISA. Co-cultured Caco-2/HT-29 cells were also grown on culture slides and treated for 24 hours with 50, 200, 500 and 5000uM AR. Cells were fixed and immunofluorescently stained with antibodies against tight junction proteins (Zonulin-1, occludin and claudin-4), cell cycle markers (Cyclin-A and p27/Kip1) and Sucrase-Isomaltase (a disacharidase).

Results/Discussion: Cell proliferation was significantly decreased after 24 hour treatment of AR ($p=0.0001$) and KBrO3 ($p=0.0065$) in a concentration dependent manner compared to controls. IL-6 and IL-8 levels were significantly increased in AR treated cells, indicating an inflammatory response ($p=0.01$). Claudin-4 expression was decreased showing that the membrane integrity was compromised with AR treatment. Cyclin-A expression was decreased while p27/Kip1 expression was increased, suggesting hindrance of cell cycle progression.
Conclusion: AR and KBrO3 significantly decreased cell proliferation and induced inflammation. Impaired function of intestinal tight junctions also occurred with AR exposure. Food additives may cause chronic intestinal inflammation and may be a contributing factor in the rise of the incidence of IBD.

210 FECAL ASCA MEASUREMENTS ARE USEFUL IN THE EVALUATION OF PEDIATRIC PATIENTS WITH CROHN DISEASE. Vivian Tang1, Clarissa Valim2, Rajat N. Moman1, Ashley Richman1, Jin Zhou3, Veena Ramgopal4, Rachel Albert4, James H. Boone4, Paul A. Rufo1, 1Center for Inflammatory Bowel Disease, Boston Children's Hospital, Boston, MA; 2Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA; 3TechLab Inc, Blacksburg, VA; 4Biostatistics, Harvard School of Public Health, Boston, MA

Background: Elevated serum anti-Saccharomyces cerevisiae antibody (ASCA) titers have been observed in patients with Crohn Disease (CD). We hypothesize that secretion of ASCA antibodies into the GI tract may be a non-invasive method of evaluating patients for CD.

Aim: We compared fecal and serum ASCA levels in patients with known or suspected Inflammatory Bowel Disease (IBD).

Methods: 114 patients including 83 with CD were included in this study. Early disease was defined as a diagnosis of IBD for 6 months or less, and active disease was defined as treatment with steroid therapy. Samples were analyzed in a blinded fashion using a quantitative enzyme-linked immunoassay. Data analysis included Student's t-test for P-values (P) and Receiver Operator Curve (ROC) with Area Under the Curve (AUC) analysis.

Results: Median serum and fecal ASCA levels were higher in subjects with CD compared to those without CD (P = 0.0008 and 0.04). The AUC-ROC for serum and fecal ASCA were 0.74 and 0.62, respectively. Among patients with active disease, serum and fecal ASCA titers were higher (P=0.007 and 0.004, respectively) in patients with CD relative to those without CD. Similarly, serum and fecal ASCA titers were higher (P=0.01 and 0.001, respectively) in patients with early diagnosed CD relative to those with recently diagnosed non CD. The AUC-ROC of fecal and serum ASCA for early disease was 0.77 and 0.79, respectively versus 0.55 and 0.74 respectively for patients having a diagnosis > 6 months.

Conclusions: ASCA titers are detectable in patients with IBD and are associated with CD. Serum ASCA showed a higher overall sensitivity for CD, whereas fecal ASCA may be superior for identifying patients with early/active CD.

211 ROLE OF X-LINKED INHIBITOR OF APOPTOSIS PROTEIN (XIAP) IN MUCOSAL IMMUNE REGULATION. Bhaskar Gurram1, Hammalev Erin2, James W. Verbsky1, 1Department of Pediatrics, Division of Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; 2Department of Pediatrics, Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI

Background: Failure to regulate immune responses in the GI tract results in IBD. X-linked lymphoproliferative disorder type-2 is caused by mutations in gene coding for XIAP, and about 17% of these patients present with early-onset severe IBD. XIAP is an inhibitor of apoptosis but is also required for NOD2 and TGF-β signaling. We hypothesize that decreased TGF-β responsiveness of T cells due to XIAP deficiency results in the development of colitis, due to a failure in the generation, survival or function of T regulatory (Treg) cells.

Methods: To induce colitis, 4x105 naïve T lymphocytes(CD4+CD25-CD45RBhi) from XIAP-/- or WT mice were injected i.p. into RAG1-/- mice and weight loss followed. To prevent colitis, 2x105 Treg cells from WT or XIAP-/- were co-injected with WT naïve T lymphocytes in to RAG1-/- mice. Mice were sacrificed when they demonstrated 20% weight loss or appear clinically sick. Lymphocytes from mesenteric lymph nodes (MLN) were analyzed for CD4, CD25, Foxp3, IL-10, TNF-α, IFN-γ and IL-17.

Results: Mice with colitis induced by XIAP-/- CD4 cells in comparison to WT CD4 cells, showed no difference in percentage weight loss, survival, or colitis scores. In this model Foxp3+ Tregs are induced in vivo, but no difference in Foxp3+ numbers was observed between WT and XIAP-/- mice.

We did not detect any difference in the ability of Treg cells from XIAP-/- or WT mice in preventing colitis. Cytokine profiles between the two groups were similar, with the exception of IL-17 producing CD4 cells that were significantly higher in RAG1-/- mice receiving Tregs from WT compared to XIAP-/- mice.

Conclusions: In an immune mediated mouse model of IBD, there was no difference in severity of colitis induced by XIAP-/- CD4 cells, nor in the ability of XIAP deficient Tregs to prevent colitis. This would argue that XIAP is not required in CD4 cells or Tregs in regulating inflammation at mucosal surfaces. Our future studies will examine the role of XIAP in non-lymphoid tissues.

212 UTILIZATION TRENDS OF INFlixIMAB AND ADAlimUMAB ASSOCIATED WITH HOSPITALIZATION AND ABDOMINAL SURGERY RATES IN INFLAMMATORY BOWEL DISEASE. K. T. Park, Aaron Sin, May Wu, Dorsey Bass, Jay Bhattacharya, Stanford University, Palo Alto, CA

Use of biologics may be associated with decreasing hospitalization and abdominal surgery in IBD, while pediatric utilization trends are incompletely characterized. We aimed: To determine potential differences in hospitalization and surgery rates associated with infliximab and adalimumab utilization trends for children and adults with IBD. To
compare the effectiveness of infliximab and adalimumab on reducing hospitalization and surgery. Longitudinal data were extracted from the STRIDE Database between the times of 2006 to 2012. Qualitative time series analysis was performed. Utilization quotients (# patients hospitalized or had surgery per quarter/total encounters per quarter) were calculated. Results showed 438 pediatric and 2,582 adult IBD patients generated a total of 51,882 inpatient and outpatient encounters. 1,185 patients had Crohn's disease; 1,531 with ulcerative colitis; 236 with indeterminate colitis. Hospitalization quotients declined for adults and children from 2007,Q1 to 2011,Q1: 0.24 to 0.16 in adults and 1.14 to 0.57 in children. Time series analysis using median spline and mean fitted plots showed downward hospitalization trends from 2006 to 2012 (P < 0.01). Trends in surgeries per quarter increased from 2006 to 2012. Utilization of infliximab increased from 2006,Q1 until 2009,Q1, but has decreased since. Adalimumab use increased since 2007 Q2. Regression models show that children had increased risk for hospitalization (OR 3.95, 95% CI 3.71-4.22), but decreased risk for surgery (0.52, 95% CI 0.42-0.64). The use of infliximab showed a protective effect for hospitalization (OR 0.63, 95% CI 0.58-0.68) and surgery (0.76, 95% CI 0.61-0.95), while adalimumab use lowered hospitalization (OR 0.74, 95% CI 0.68 - 0.80) but had higher odds of surgery (OR 1.46, 1.16 - 1.83). In conclusion, hospitalization rates for IBD show downward trends, not reflected in surgery rates. Infliximab and adalimumab use is associated with lower hospitalization rates, with infliximab use also linked to lower risk for surgery.

213 PEDIATRIC CAPSULE ENDOSCOPY: SINGLE CENTER EXPERIENCE. Khiet D. Ngo, Carla Perez, Marquelle Klooster, Sally Rajcevich, Lynne Yulip-Lopez, Samantha Stephenson, Manoj Shah, Pediatrics, Loma Linda University School of Medicine, Loma Linda, CA
AIM: Describe CE experience in a large cohort.
METHODS: Retrospective review of patients 1-19yr who underwent CE from 2005-2011. Outcomes were based on small bowel (SB) findings and defined as: Diagnostic (CE findings answered/explained original clinical indications/symptoms) or Non-Diagnostic (CE findings did not answer/explain clinical indications/symptoms).
RESULTS: 320 studies were performed in 278 patients. Demographics: 50% females, Mean age=13.6y (SD3.5 range). Median transit times: Gastric=31min (1-396min) and SB=211min (23-452min). Indications for CE: 36.4% suspected IBD, 25.2% follow-up known IBD, 2.5% suspected celiac, 1.2% follow-up known celiac, 10.3% non-specific abdominal pain, 14.5% GI Bleed, 0.9% non specific diarrhea, and 4.4% polyposis evaluation. Study outcomes: 62% non-diagnostic, 38% diagnostic. 77% of all patients ingested the capsule. 82% of studies were complete (reached TI/cecum). One teenager with crohn's required surgery for retained capsule. 82% of studies had images adequate for interpretation; dark fluid was the most common reason for inadequate image visualization. 55 studies were in children <10yr. Youngest patient: 1.5yr. In 25 studies in children <10yr the capsule was ingested; youngest child to ingest a capsule=5yr.
CONCLUSIONS: CE is feasible in children as young as 1.5yr. Children as young as 5yr can safely swallow the capsule endoscope. Diagnostic yield for CE is highest for patients undergoing polyposis evaluation, follow up celiac disease, and follow up IBD. Diagnostic yield of CE in our series is lower than in previously reported studies. Patient selection is important to optimize diagnostic yield in CE.

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>DIAGNOSTIC YIELD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyposis</td>
<td>93%</td>
</tr>
<tr>
<td>Follow Up Celiac</td>
<td>75%</td>
</tr>
<tr>
<td>Follow Up IBD</td>
<td>20%</td>
</tr>
<tr>
<td>Suspect GI Bleed</td>
<td>17%</td>
</tr>
<tr>
<td>Suspect Celiac</td>
<td>12%</td>
</tr>
<tr>
<td>Suspected IBD</td>
<td>8.5%</td>
</tr>
<tr>
<td>Non specific abdominal pain</td>
<td>6%</td>
</tr>
<tr>
<td>Non-Specific Diarrhea</td>
<td>0%</td>
</tr>
</tbody>
</table>
214 THE EFFECTIVENESS AND MECHANISM OF A TRADITIONAL CHINESE HERBAL FORMULATION FOR CROHN'S DISEASE. David Dunkin1, Ying Song2, Stephanie Dahan3, Keith Benkov4, Xi-Min Li5, Lloyd Mayer6, 1Pediatric Gastroenterology, Mount Sinai School of Medicine, NY, NY; 2Immunology Institute, Mount Sinai SOM, NY, NY; 3Pediatric Allergy and Immunology, Mount Sinai SOM, NY, NY

Purpose: The prevalence of Crohn's disease (CD) is increasing. Current therapies can have serious side effects. FAHF-2 is based on a traditional Chinese herbal formula that has long been used to treat colitis. We sought to investigate its anti-inflammatory effects and mechanism of action.

Methods: A CD45RBHi transfer model of colitis was used to assess the effectiveness of FAHF-2. The effect of FAHF-2 on TNF-α production was assessed in vitro and activation of NF-κB in LPS-stimulated RAW264.7 cells determined by western blot. PBMCs from 26 CD children and 17 non-IBD children were cultured with or without FAHF-2 in the presence or absence of LPS. Cytokines and chemokines were measured by multiplex immunoassay. The effect of FAHF-2 on TNF-α producing monocytes and T cells was determined by flow cytometry.

Results: FAHF-2 treatment in a murine model of colitis decreased weight loss (11.3% vs. 19.2%, p<0.05), inflammation (p<0.05), and TNF-α and IFN-γ production by anti-CD3/28 stimulated splenocytes and MLNs (p<0.05). Pre-incubation of RAW267.4 cells with FAHF-2 decreased TNF-α in a dose dependent manner and decreased IκB-α phosphorylation (p=0.001), IκB-α degradation (p=0.001) and AKT phosphorylation (p<0.01). Increased TNF-α was detected in PBMC cultures stimulated with LPS from CD subjects as compared with non-IBD subjects. FAHF-2 treatment reduced LPS-induced TNF-α, IL-12, IFN-γ, IL-2, IP-10, MIG, and MIP-1β, and increased GM-CSF production by PBMCs from CD subjects (n=14). FAHF-2 reduced the number of TNF-α+CD14+ monocytes and TNF-α+CD3+ T cells in stimulated PBMCs from CD.

Conclusion: FAHF-2 was effective in a murine model of IBD. It inhibited pro-inflammatory cytokine production and the number of TNF-α+CD14+ monocytes and TNF-α+CD3+ T cells in PBMCs from CD children. FAHF-2 inhibition of TNF-α production may be due to blocking the NF-κB pathway. Further clinical investigation of FAHF-2 for the treatment of CD is warranted.


Background: Infliximab (IFX) is commonly used to treat Inflammatory Bowel Disease (IBD). IFX is supplied in 100mg vials and remains expensive. Dosing usually starts at 5mg/kg, and is commonly rounded up or down. The scope of dosing practices is unknown. Under-dosing may place patients at risk for exacerbation of IBD. Over-treatment potentially carries increased risk of infectious and malignant complications. We aimed to characterize IFX dosing practices among pediatric IBD practitioners participating in the ImproveCareNow Network.

Methods: We distributed a survey to pediatric IBD practitioners from March to December 2011. Data were manually entered by two researchers in SPSS. Double data reconciliation and analyses were performed with Stata.

Results: 207 of 287 responded (72.1%), including 179 attending physicians, 26 nurse practitioners and 1 physician assistant. 37.7% (78/207) of respondents indicated that their practice has no uniform approach to rounding doses. Of 97 with uniform approach, 50.5% (n=49) always round up to the nearest 100mg, 38.1% (n=37) round up or down to the nearest 100mg and 6.1% (n=6) round up or down by a smaller increment (20-50mg). If the dose is escalated, 68.6% (142/207) increase directly to 10mg/kg, whereas 22.2% (46/207) increase to an intermediate dose. All 31 practices infuse IFX over ≥2hr duration. 11 practices (35.5%) also infuse over <2hr, including 3 practices (9.7%) that perform 1hr duration infusions. Regarding the practice of steroid premedication prior to IFX infusion, 28.6% of respondents (59/206) always premedicate and 12.1% (25/206) never premedicate. Of the 114 indicating “it depends”, 94.7% (n=108) premedicate if there has been a prior infusion reaction, 11.4% (n=13) premedicate if giving IFX monotherapy, 40.4% (n=46) premedicate if human anti-chimeric antibodies are present and 45.6% (n=52) premedicate if there has been a prolonged lapse between treatment doses. Conclusion: There is wide variation in practice patterns of infliximab dosing for pediatric IBD. The impact of dosage rounding and escalation on outcomes remains unclear.

216 Enteric Infections in Hospitalized Pediatric Patients with Inflammatory Bowel Disease. Narendra Vadamudi, Meredith C. Hitch, Kirk A. Thame, Reed Dimmitt, Carrie Huisengh, Jeanine Maclin, Children's of Alabama, UAB, Birmingham, AL

Introduction: Intestinal infections in patients with inflammatory bowel disease (IBD) may complicate the clinical picture and trigger IBD flares. The incidence of infection from enteropathogens in hospitalized pediatric patients with IBD flare has not been formally assessed. The aim of this study is to assess the incidence of enteric infections and to evaluate their impact on the clinical outcome in hospitalized pediatric IBD patients.

Methods: Medical records of all patients admitted with a acute flare of IBD between 2003-2010 were reviewed retrospectively. IBD patients admitted with relapse and stool studies performed at admission were included; those with negative stool studies were used as control. Short (< 30 days) and long term (<1 year) outcomes following
INDEX admission were measured.
Results: We observed 92 IBD relapses requiring hospitalization in 59 eligible patients during the study period. Enteric infection was found 24% of all relapses (22 episodes, 14 patients with UC and 8 with CD). Clostridium difficile infection (CDI) was the most common (12/22, 54%), with a prevalence of 13% of all relapses. Cryptosporidium (4), Salmonella (4), Shigella (1) and Calci virus (1) were the other organisms isolated. Compared to controls, patients with infection were younger (p = 0.02) and recently diagnosed (p = 0.01); whereas, no statistically significant difference was found in outcomes measured by readmissions, escalation of therapy, or the need for surgery. In evaluating the impact of specific pathogens on the natural course of IBD, patients with CDI and non-CDI were compared. CDI was predominant in patients with UC (p = 0.07). No significant differences in short term outcomes were observed; however, patients with CDI were more likely to have readmission (p = 0.03) and escalation of therapy (p = 0.01) within one year following index admission. 25% of patients with CDI also required colectomy in the year following infection.
Conclusion: Enteric infections are common in pediatric IBD patients presenting with diarrheal relapse. CDI can be associated with aggressive disease course leading to increased need for readmission and escalation of therapy in the year following infection.

217 RECTAL MicroRNA LEVELS ARE ALTERED IN PEDIATRIC UCLeRATIVE COLITIS.
Adam M. Zahm, Robert N. Baldassano, Joshua Friedman, Pediatrics, Division of Gastroenterology and Nutrition, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

The two predominant inflammatory bowel diseases (IBD), Crohn disease and ulcerative colitis, are characterized by an abnormal, chronic immune response affecting the gastrointestinal tract. Understanding the dysregulation of signaling networks that leads to chronic intestinal inflammation will aid the development of therapeutics and lead to improved patient outcome.

MicroRNAs (miRNAs) are short ribonucleotides that decrease target mRNA stability and inhibit translation and are known to regulate immune cell development and function. Altered tissue miRNA profiles have previously been reported in the intestinal epithelia of adult IBD patients, yet approximately one-third of newly diagnosed IBD patients are under the age of 18.

To identify miRNAs dysregulated in pediatric IBD, we performed a pilot study of intestinal miRNA in patients undergoing endoscopy for suspicion of IBD. A screen of miRNA levels was performed in rectal biopsies from patients with active Crohn disease or ulcerative colitis and matched controls (n=6 each) using the NanoString nCounter platform. Several miRNAs abundantly expressed in colonic epithelia, including miR-192 and miR-194, were decreased more than two-fold in ulcerative colitis compared to Crohn disease and controls. Additionally, miRNAs associated with immune cell populations, including miR-142-3p and miR-146a, were significantly elevated in ulcerative colitis. No significant differences in miRNA levels were observed between Crohn disease and control samples. The results of our screen were subsequently confirmed using quantitative RT-PCR. These findings suggest that pediatric ulcerative colitis is associated with an altered rectal miRNA profile. Future work may identify crucial miRNA:mRNA interactions necessary for immune homeostasis in the colon.

218 CALCIUM-SENSING RECEPTOR IN THE GUT: EVIDENCE FOR ITS ROLE IN MEDIATING KNOWN NUTRITIONAL THERAPY OF INFLAMMATORY BOWEL DISEASE. Sam Cheng, 1Yale University, New Haven, CT; 2University of Florida, Gainesville, FL

Total or exclusive enteral nutrition (TEN) is an effective primary therapy for Crohn's disease in children and adolescents; the mechanism of its action has not been elucidated. The extracellular calcium-sensing receptor (CaSR) is a unique G protein-coupled receptor that functions as a sensor of specific nutrients such as calcium, some amino acids and oligo-peptides, and polyamines by interacting with these molecules as its ligands. CaSR is highly expressed in the epithelium lining the mucosa of the gastrointestinal tract as well as several other cell types including the subepithelial myofibroblasts, the antigen-presenting macrophages/monocytes and the enteric nervous system. This pattern of distribution prompts us to hypothesize that CaSR plays a central role in regulating intestinal fluid secretion, inflammation and mucosal healing. To test this hypothesis, 28-day old prepubertal male Sprague-Dawley rats were fed 2 weeks with control diet or diet enriched in a selective CaSR agonist calcium, tryptophan or spermine before 1.5-5% dextran sodium sulfate (DSS) was added via drinking water to induce colitis. Animals continued on indexed diet and DSS either for 7 days to induce "acute" colitis or for two cycles of 5 day-on and 2 day-off to induce "chronic" colitis. Our preliminary data show that animals fed with a diet enriched in calcium (2.5 x normal) had significantly less severe diarrhea, reduced clinical and histological severity of colitis, accelerated rate of mucosal healing and improved overall growth and nutrition. A similar inflammation-inhibitory effect was also observed for tryptophan (2.5x)- and spermine (2.5x)-enriched diet groups. It is concluded that dietary supplementation of CaSR agonist calcium, spermine and/or tryptophan may be beneficial in the prevention and/or treatment of IBD. Future studies in further delineating the unique role of CaSR would help optimize the use of CaSR agonists in combination with known nutritional therapy to treat Crohn's disease as well as other intestinal inflammatory diseases in children.
219 NEW ASSAY TO DETECT INFlixIMAB LEVELS AND ANTI-INFLIXIMAB ANTIBODIES FROM A SINGLE SERUM SAMPLE IS USEFUL IN MEASURING EFFICACY OF TREATMENT WITH INFlixIMAB IN CHILDREN WITH IBD. Jess Kaplan1, Gabor Veres2, Elisabeth De Greef2, Emil Chuang4, S. Lockton2, Doloresz Szabo2, KrisztaMoharo2, Linda Ohrmund4, Scott Hauenstein4, Sharat Singh1, Andras Arato1, G. Veereman-Wauters1, Harland S. Winter2, 1MassGeneral Hospital for Children, Boston, MA; 2Semmelweis University, Budapest, Hungary; 3UZB, Brussels, Belgium; 4Prometheus Laboratories, San Diego, CA
Introduction: Anti-infliximab antibodies (ATI) and serum infliximab (IFX) levels are increasingly implicated in the efficacy and safety of IFX therapy in patients with inflammatory bowel disease (IBD). The most common method for detection of ATI is a double-antigen ELISA utilizing IFX for ligand and detection antibody. In this assay, the presence of serum IFX interferes with ATI measurement, limiting its ability to detect ATI and IFX from the same serum sample. A new fluid phase mobility shift assay for IFX and ATI detection may be less amenable to this interference, allowing for measurement of both IFX and ATI from the same serum sample. Study Population: IFX and ATI were measured in 230 serum samples from 71 children (Group I) with IBD (ages 7-21 years) using a new fluid phase mobility shift assay. All children were treated with standard induction at 0, 2, 6 weeks with 5 mg/kg IFX. A subset of 31 children (Group II) had serial ATI and IFX level samples drawn prior to infusions. Results: ATI were detected in 47 of 230 samples (range 0.28 to >800 U/ml) and in 21 of 71 children (29.5%). In the 47 samples with detectable ATI, 8 had measurable IFX (range 0.77-19.27 ug/mL). In Group II analysis, 8/31 (25.8%) patients were ATI+. The median IFX levels for ATI+ (n = 30) and ATI- (n = 154) samples were 0 µg/ml and 2.55 µg/ml respectively (p = <0.0001). ATI+ patients had higher C-reactive protein levels than ATI- patients but there was no correlation between ATI status and PCDAI. Conclusions: A significant number of children treated with IFX developed ATI. The new fluid phase mobility shift assay is effective at measuring both IFX and ATI in the same serum sample. Simultaneous monitoring of IFX level and ATI may improve therapeutic decisions. Supported in part by a grant from the Pediatric IBD Foundation

220 ILEAL MUCOSA-ASSOCIATED MICROBIOTA CHANGES IN CHILDREN WITH NEWLY DIAGNOSED, TREATMENT-NAÏVE CROHN’S DISEASE. Jess Kaplan1, M. Bhasin2, B. D. Gold3, B. S. Kirschners4, N. L. Ward5, S. A. Cohen6, M. B. Heyman6, G. D. Ferry7, R. N. Baldassano8, C. J. Moran1, B. Steven9, E. A. Garnett4, M. P. Tierney4, L. Drake1, S. E. Dowd9, S. B. Cox9, S. A. Mir7, R. Kellermayer1, T. A. Libermann1, H. S. Winter2, 1MassGeneral Hospital for Children, Boston, MA; 2BIDMC, Boston, MA; 3CCDHC, Atlanta, GA; 4U. Chicago, Chicago, IL; 5U. Wyoming, Laramie, WY; 6UCSF, San Francisco, CA; 7TCH, Houston, TX; 8CHOP, Philadelphia, PA; 9Pathogen Research, Lubbock, TX
Background: Altered gut microbiota have been linked to the pathogenesis of inflammatory bowel disease (IBD), but the microbiome may be altered by therapy and disease duration. We report differences in ileal mucosa-associated microbiota among children with newly diagnosed, treatment-naïve, Crohn's Disease (CD), Ulcerative Colitis (UC) and non-IBD controls. Methods: Ileal mucosal biopsies were obtained from 72 children (ages 2-17) undergoing ileocolonoscopy for evaluation of possible IBD. Bacterial community structure was determined by 454 Pyrosequencing of 16S ribosomal RNA genes. Shannon Diversity Index and Principal Coordinates Analysis (PCoA) were used to compare differences in microbiota between groups. Results: We studied 23 patients with newly diagnosed/treatment naive IBD (17 CD & 6 UC) and 49 non-IBD controls. The mean number of Operational Taxonomic Units (OTU) per ileal sample was 5085 (range 764-12403). There was reduced ileal microbial diversity in CD patients compared to both UC and controls. PCoA of unweighted UniFrac distances showed marked differences in ileal microbiota structure in CD patients compared to both UC and controls. Two bacterial taxa were significantly depleted in CD subjects; a Firmicute from the genus Roseburia (p = 0.0002) and a Bacteroidetes from the genus Prevotella (p = 0.0001). Conclusions: We identified significant alterations in microbial diversity and composition in the ileal mucosa of treatment-naive children with CD. Ongoing analyses may lead to further insight into the role of specific gut microbes or microbial communities in the pathogenesis of pediatric IBD. Supported in part by The Pediatric IBD Foundation and the NIH

221 THE ASSOCIATION OF LYMPHOCYTIC ESOPHAGITIS WITH PEDIATRIC CROHN’S DISEASE. Dyer Heintz1, Lisa Sutton2, Arthur Weinberg2, Ashish S. Patel1, 1Pediatric Gastroenterology, UT Southwestern, DALLAS, TX; 2Pediatric Pathology, UT Southwestern, Dallas, TX
Lymphocytic esophagitis (LE) is an increasingly common finding in esophageal biopsies, but the significance remains unknown. LE is generally characterized as an elevation in intraepithelial lymphocytes with a relative paucity of granulocytes. While its clinical significance has not yet been established, some experts have hypothesized LE is associated with Crohn's disease (CD).

To discern whether there is a higher prevalence of LE in patients with CD, a single pathologist reviewed esophageal biopsies on 580 consecutive biopsies of 545 children undergoing upper endoscopy at a tertiary children's hospital over one calendar year. LE was defined as greater than 50 intraepithelial lymphocytes per high power field with a paucity of granulocytes. Thirty-one patients met criteria for LE for an overall prevalence of 5.7%. We performed a
retrospective chart review to obtain the history, patient information (i.e. age, sex), allergies, diagnoses, length of follow up and other information of these patients. The patients with LE and CD were compared with those who had LE and non-CD diagnoses.

Patients with CD accounted for 49 of the 545 patients. Of the 31 total patients meeting criteria for LE, 6 had CD and 25 had other non-CD diagnoses. The prevalence of LE in patients with CD was 12.2% versus 5% in the non-CD population (p<0.05). The mean intraepithelial lymphocyte counts in patients with LE and CD was 188.3 as opposed to 88.2 in patients with LE and non-CD diagnoses (p<0.05). These findings conclude pediatric patients with CD do have a higher prevalence of LE than patients without CD. Those patients with higher numbers of lymphocytes per high power field are also more likely to have CD. The most common associated symptoms were abdominal pain (48%) and vomiting (39%) among all patients with LE. No statistical differences were noted in age, sex, symptoms or medications between the two groups.

222 NEUTROPHIL PRIMING IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE.

Melissa Jensen, Emily Gross, Brianna Hilkin, Riad Rahhal, Jessica Moreland, University of Iowa, Iowa City, IA

Inflammatory bowel disease causes significant morbidity worldwide including the pediatric population. This chronic inflammatory condition can include systemic manifestations, with neutrophils (PMNs) and the circulating cytokine TNF-α as potential mediators in this process. Although PMNs are unequivocally required for microbial killing, they can also cause host tissue damage secondary to inappropriate activation. PMN priming is an intermediate state of activation whereby exposure to a priming stimulus enhances responsiveness to subsequent stimuli. Priming is elicited by host and bacterial products, including TNF-α. Priming occurs both in vitro and in vivo. PMN priming has recently been demonstrated to occur in chronic inflammatory diseases. We hypothesized that circulating neutrophils from pediatric patients with IBD display a primed phenotype, and that the degree of priming correlates with the extent of their disease activity. After IRB approval and informed consent, neutrophils were isolated from pediatric IBD patients and age-matched controls. Clinical disease activity indices and medication information were also collected. Neutrophil priming phenotypes were characterized by analysis of NADPH oxidase activity, cell surface protein expression and elastase release. Priming of respiratory burst was significantly increased in all patients with IBD compared to controls, with Crohn's disease patients demonstrating a 1.5-fold increase of NADPH oxidase activity in response to fMLF. Analysis of cell surface marker expression showed increased expression of CD11b in patients with Ulcerative Colitis as compared to control patients. Elastase release from primary granules was studied as an additional endpoint of priming, and IBD patients also displayed a greater priming of elastase release. In summary, neutrophils from pediatric patients with IBD display a primed phenotype that includes enhanced ROS generation, increased cell surface protein expression and elastase release. We speculate that PMN priming during IBD may contribute to host tissue damage and patient morbidity.

223 DECREASED EXPRESSION OF INTESTINAL ALKALINE PHOSPHATASE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE.

Diana G. Lerner1, Nita Salzman1, Katherine Fredrich2, Hayward Michael1, Michael Stephens1, Bhaskar Gurram1, Vince Biank1, Pippa Simpson3, David Gourlay2, 1Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Surgery, Medical College of Wisconsin, Children's Research Institute, Milwaukee, WI; 3Quantitative Health Science, Medical College of Wisconsin, Milwaukee, WI

Inflammatory bowel disease (IBD) is a chronic, inflammatory condition of the gastrointestinal tract with the highest incidence in pediatric patients occurring in childhood and early adolescence. The pathophysiology of IBD is thought to involve abnormal activation of Toll Like Receptor (TLR) pathways in response to bacterial antigens such as bacterial lipopolysaccharide (LPS). Intestinal alkaline phosphatase (IAP) is a small intestinal brush border enzyme, which dephosphorylates LPS rendering it inactive and incapable of TLR4 activation and cytokine production. IAP is believed to preserve normal gut homeostasis. IAP is expressed in lower amounts in colonic tissue of patients with Crohn's disease (CD) and Ulcerative Colitis (UC) and has shown promise in early clinical trials for treatment of steroid dependent UC. The aim of this study was to compare IAP mRNA expression in terminal ileum (TI) samples of pediatric IBD verses non-IBD patients.

Methods: All pediatric patients undergoing colonoscopy at our institution were approached for enrollment after IRB approval. At the time of colonoscopy biopsies were collected from the terminal ileum. IAP gene expression was measured by Real Time-PCR on terminal ileal tissue as determined by plasmid standard curve with GAPDH used as an internal control. Statistical analysis: Mann-Whitney test.

Results: A total of 116 pediatric (up to 18 years old) patients were enrolled, 36 with CD, 12 with UC and 68 controls. IAP expression is significantly lower in CD (p<0.04) and in UC (p<0.004). There is significant variability of IAP expression between patients in the control and CD groups, but not in the UC patients. IAP expression is significantly decreased in CD in the presence of TI inflammation (P<0.01) but is low in UC irrespective of TI histology.
Discussion: IAP expression in pediatric patients with IBD is significantly decreased compared to controls. Patients with UC have less variability in IAP expression. Loss of IAP may be most significant in the colon due to higher LPS load. Decreased IAP may play an important role in regulating intestinal inflammation in pediatric IBD patients especially in patients with UC.

224 CROSS-SECTIONAL IMMUNITY BETWEEN HEPATITIS A, HEPATITIS B, AND VARICELLA IN IBD. Vesta Salehi, Robbyn Sockolow, Aliza Solomon, Pediatric Gastroenterology, Cornell Medical College, New York, NY

Background: Few studies have examined immune response with respect to individual vaccines in subjects with IBD. Patients with IBD may be at increased risk for infection including vaccine-preventable diseases. The aim of our study is to evaluate for an association between non-immunity amongst multiple vaccine preventable viruses.

Methods: This is a retrospective chart review of all patients seen in our practice with the diagnosis of IBD from 2007 to 2011. Evidence of serologic immunity or non-immunity was identified with use of antibody titers to different viruses.

Results: A total of 119 subjects with IBD and history of immunization or disease with one of the 3 viruses were identified. A total of 112 had hepatitis A serology with 55.4% being non-immune. A total of 117 had hepatitis B serology with 30.8% being non-immune. A total of 110 had varicella antibodies checked with 20.9% being non-immune. P value < 0.0001 by chi test indicating rates of non-immunity differ between the three vaccines. The concordance between non-immunity for one vaccine and non-immunity for other vaccines was assessed by kappa statistics. There is no concordance between non-immunity between the three vaccines: Hepatitis A and Hepatitis B with kappa = 0.04, P=0.63, hepatitis A and Varicella with kappa = 0.03, P=0.70, hepatitis B and Varicella kappa = 0.05, P=0.57.

Conclusions: Patients with inflammatory bowel disease are commonly placed on immunosuppressive medications making it important to screen for vaccine preventable diseases. In our population, a significant proportion of patients lacked immunity necessitating re-vaccination. There was no significant way to predict which virus patients lacked immunity to and therefore all should routinely be checked.

Association between Non-Immunity and Type of Vaccine

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Non-Immune</th>
<th>Immune</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>62 55%</td>
<td>50 45%</td>
<td>112</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>36 31%</td>
<td>81 69%</td>
<td>117</td>
</tr>
<tr>
<td>Varicella</td>
<td>23 21%</td>
<td>87 79%</td>
<td>110</td>
</tr>
<tr>
<td>Total</td>
<td>121 36%</td>
<td>218 64%</td>
<td>339</td>
</tr>
</tbody>
</table>

225 IMPACT OF ALEXITHYMIA ON DISEASE-SPECIFIC QUALITY OF LIFE IN ADOLESCENTS WITH IBD. Jaime D. Crowley1, Gabriela M. Reed2, Crista E. Wetherington1, Ashish Patel1, Sunita Stewart1, Stephen Robertson1, Lauren C. Smith1, 1UT Southwestern Medical Center, Dallas, TX; 2Psychiatry, Children's Medical Center, Dallas, TX

In adolescents with Inflammatory Bowel Disease (IBD), the psychological variables that contribute to health outcomes (i.e., disease-specific quality of life, illness course, and disease severity) remain relatively unstudied. Both depression and stress have been implicated in adult IBD health outcomes. Alexithymia, defined as both a personality trait and affective deficit disorder, may represent another psychological variable influencing IBD health outcomes. Higher rates of alexithymia have been documented and associated with poorer quality of life (QOL) in adult IBD populations. Recent research shows significant rates of alexithymia among adolescents with IBD. This study examined the relationship between alexithymia, other psychological variables (i.e., depressive symptoms and perceived stress), and health outcomes. An investigation of 63 participants with IBD between the ages of 13 to 17 years revealed that all of the psychological variables were significantly and inversely correlated with disease-specific QOL. Notably, alexithymia emerged as the strongest predictor of disease-specific QOL and consistently accounted for more unique variance than depressive symptoms and perceived stress. None of the psychological variables were significantly related to illness course, and only perceived stress of major life events was significantly correlated with disease severity. Disease severity was also significantly correlated with disease-specific QOL; however, this relationship was mediated by perceived stress of major life events. Taken together, the present results implicate alexithymia as a risk factor for poor illness perception and adjustment in adolescents with IBD. The potential lifelong repercussions of alexithymia make it an important topic for health outcome research, which may bear implications for future interventions.
226 RECTAL LIPOMA IN A PEDIATRIC PATIENT WITH INFLAMMATORY BOWEL DISEASE.
Sameer Lapsia, Julie Khlevner, Anupama Chawla, Jeffrey Morganstern, Pediatric Gastroenterology & Nutrition, Stony Brook Children's Hospital, Stony Brook, NY
Gastrointestinal manifestations of inflammatory bowel disease, especially Crohn's disease include inflammation, edema, pseudopolyps, strictures, and stenosis. We present the first case of a rectal lipoma in a patient with inflammatory bowel disease and one of very few cases reported in children. Case report: This is a 16 year old female with Crohn's disease complicated with perineal fistulas, joint pain, episcleritis, and erythema nodosum. Due to worsening disease despite being on maximized medical therapy the patient underwent a colonoscopy to assess the full extent of her disease and determine if surgical intervention would be an option. At approximately 10 cm from the anal opening, a smooth, polypoid mass 1.5 cm in diameter with a 1 cm base was noted protruding into the lumen. Due to concerns for a possible cancerous lesion, the polypoid mass was resected. The large base of the mass in our patient warranted a 2-step procedure, firstly achieving hemostasis with the endoloop followed by snare cautery of the polypoid mass. Pathology diagnosed the mass to be a lipoma. No malignant characteristics were noted. Discussion: Colonic lipomas are soft tissue tumors originating from mature adipocytes. Although rare, they are the second most common benign tumor of the colon after adenomatous polyps with an incidence ranging between 0.2% and 4.4% with no cases reported in patients with inflammatory bowel disease. Resection of these masses is essential due to complications arising from lesions larger than 2 cm such as abdominal pain, change in bowel pattern, massive bleeding, obstruction, intussusception, or perforation. Cases of these lipomas metamorphosing into liposarcomas have been reported making removal of this lesion a necessity. Conclusion: Lipomas must be considered as part of the differential diagnosis when a colonic polypoid lesion is encountered in patients with inflammatory bowel disease.

227 INFUSION AND POST-INFUSION REACTIONS TO INFLIXIMAB IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS. Tracey Procopi, Ann Zimmerman, Andrew Grossman, Robert N. Baldassano, Children's Hospital of Philadelphia, Philadelphia, PA
Objective: According to manufacturer guidelines, infliximab infusions should be followed by a monitoring period at the infusion site. Though prior studies have examined the incidence rate of infliximab reactions in pediatric IBD patients, the rate of acute reactions during the post-infusion monitoring period has not been examined. The objectives were to characterize infusion and post-infusion reactions.
Results: Of 7616 infliximab infusions given to IBD patients at CHOP, 185 acute infusion reactions were identified. 164 met the inclusion criteria. 156 reactions (2.05%) occurred during infliximab infusion; 19 were anaphylactic reactions (requiring epinephrine or oxygen administration) (0.25%). During the 30 minute post-infusion monitoring, no anaphylactic reactions and only 8 mild reactions (0.1%) occurred, with only half requiring any medical intervention.
Conclusion: Anaphylactic reaction during infliximab infusion is uncommon but can require emergent medical intervention. There were no anaphylactic reactions and only rare mild reactions during post-infusion monitoring. Elimination of the post-infusion monitoring period would not adversely affect patient safety and would reduce time burden on patients and hospitals, potentially reducing costs.
<table>
<thead>
<tr>
<th>Reaction</th>
<th># of reactions</th>
<th>Patient age</th>
<th>Concomittant meds</th>
<th>History of past reactions</th>
<th>Premeds</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (38.1-38.5°C)</td>
<td>3</td>
<td>13</td>
<td>mesalamine, 6 mercaptopurine, folic acid, multivitamin</td>
<td>no (24 prior infusions)</td>
<td>none</td>
<td>none</td>
<td>Questionable reaction. Patient prone to fevers</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td></td>
<td>mesalamine, 6 mercaptopurine, lansoprazole</td>
<td>no (21 prior infusions)</td>
<td>none</td>
<td>acetaminophen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td>mesalamine, metronidazole, multivitamin, methotrexate, folic acid</td>
<td>yes 2: temp during infusions 3 &amp; 4 yrs prior (54 prior infusions)</td>
<td>none</td>
<td>acetaminophen</td>
<td></td>
</tr>
<tr>
<td>Facial Flushing</td>
<td>1</td>
<td>13</td>
<td>metronidazole, azathioprine</td>
<td>yes- 1: fever facial flushing during infusion 7 wks prior (32 prior infusions)</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Hives</td>
<td>2</td>
<td>8</td>
<td>mesalamine, ciproflaxacin, metronidazole, lansoprazole, azathioprine</td>
<td>no (36 prior infusions)</td>
<td>none</td>
<td>diphenhydramine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td>azathioprine, balsalazide, lansoprazole, multivitamin, iron, probiotics</td>
<td>no (0 prior infusions)</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Itchy arms/legs (no rash); throat irritation</td>
<td>1</td>
<td>17</td>
<td>methotrexate, prenatal vitamin</td>
<td>yes 5: chest tightness all during infusions 5 years prior (51 prior infusions)</td>
<td>diphenhydramine</td>
<td>hydroxyzine</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>1</td>
<td>6</td>
<td>metronidazole, mesalamine, 6 mercaptopurine, lansoprazole, VSL3, prednisone</td>
<td>no (3 prior infusions)</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Post-infusion monitoring reactions.
228 ONE CENTER’S EXPERIENCE WITH HIGHLY DESTRUCTIVE PERIANAL DISEASE IN PEDIATRIC CROHN’S DISEASE. Sarah E. Catalano1, Brian Regan2, Alejandro Flores2, 1Tufts University School of Medicine, Boston, MA; 2Division of Pediatric Gastroenterology, Floating Hospital for Children at Tufts Medical Center, Boston, MA

Background: Highly destructive perianal disease (HDPD) in pediatric Crohn’s disease is a severe and debilitating condition characterized by perianal fistulas, abscesses, skin tags and fissures. The disease is often resistant to medical management and frequently requires surgical intervention. In addition, there are significant psychological sequelae associated with the unrelenting and disfiguring nature of this disease.

Methods: Retrospective review of patients with HPPD at a single institution from 2004-2006.

Results: 6 patients were included in this study (67% male). The average age of Crohn's diagnosis was 10.8 years. Perianal disease was the presenting sign in two of the patients. 83% of the patients were treated with infliximab at some point during the course of their disease. Two patients showed complete resolution of perianal symptoms in response to thalidomide treatment. One patient is doing well on adalimumab after failing balsalazide and developing transient bruising after infliximab infusion necessitating discontinuation. Another patient failed 6-MP and has shown complete response to infliximab treatment. The three remaining patients ultimately required surgical intervention for their perianal symptoms after failing various immunosuppressant agents. One patient initially had a diversion, but a proctectomy was performed 10 months later after persistence of perianal symptoms. Two of the patients ultimately had an ileostomy after failing medical treatment which resulted in the resolution of perianal symptoms.

Conclusions: The course and treatment of HDPD is highly variable. Various immunosuppressants have been used to treat HPDP, often to no avail. Despite aggressive medical management, half of the patients in this case review required surgical intervention for management of this chronic condition. Additional research and larger case reports are needed to establish the most effective management for HDPD.

229 EFFICACY OF INFlixIMAB THERAPY IN THE PEDIATRIC IBD POPULATION AND THE LIKELIHOOD OF FAILURE. Alisa Olmsted, Ian Leibowitz, Lynn Duffy, Bernadette Diez, INOVA Digestive Disease Center, Fairfax, VA

Background: Biologic therapies that target tumor necrosis factor alpha have been found to be effective in the treatment of moderate to severe inflammatory bowel disease (IBD), but efficacy in the pediatric population is still being assessed.

Objectives: 1) To assess differences between patients who failed or succeeded Infliximab therapy in the pediatric IBD population. 2) To identify measures to facilitate identification of the likelihood of success or failure.

Methods: This is a retrospective chart review. IBD patients were tracked for: age at diagnosis, months until start of therapy, duration of therapy, disease location and phenotype, and surgical intervention. Demographic differences between the success and failure groups were calculated using a 2-sample Student t-test. Statistical tests were 2-sided with equal variance, at an alpha level of 5%. A novel likelihood-of-failure measure (LF) was created by dividing months until therapy over the age at diagnosis.

Results: 41 patients were evaluated. Patients ranged from 8 to 17 years at start of therapy, with a mean of 14.2±2.3yr. 66% were male and 34% were female. 31 were diagnosed as Crohn's Disease (CD, 76%), 2 as Indeterminate Colitis (IC, 5%), and 8 as Ulcerative Colitis (UC, 19%). 29% of patients (n=12) failed therapy (9 CD, 2 UC, 1 IC) due to adverse reaction (n=6) or lack of response (n=6). There was no significant difference in any of the measures between the success and failure groups in both the IBD group, or within the disease subsets. In patients < 17yr in the CD population only, there was a significant difference (P=0.0006) in the LF measure between the success (LF=1.17±0.87) and failure groups (LF=3.41±2.04). Of the 9 CD patients that failed, disease was either ileocolonic (n=6) or colonic (n=3), with a larger proportion of stricturing (n=2) and fistulizing (n=3) phenotypes. 7 required surgical intervention.

Conclusion: Age at diagnosis and months until start of therapy, in combination, may predict failure rate in the CD population. These measures do not individually predict success.

230 OUTPATIENT NON-DRUG COSTS ASSOCIATED WITH INFlixIMAB ADMINISTRATION FOR PEDIATRIC INFLAMMATORY BOWEL DISEASE. May Wu, Aaron Sin, Fred Nishioka, K. T. Park Stanford University, Palo Alto, CA

BACKGROUND: Infliximab is the most widely used biologic agent for Crohn's disease (CD) and ulcerative colitis (UC), but requires outpatient infusion units due to its intravenous administration requirement.

OBJECTIVE: 1) To determine the average non-drug costs associated with each outpatient use of infliximab for pediatric IBD. 2) To determine the proportion of non-drug costs associated with each outpatient infliximab use relative to the total cost of each encounter.

METHODS: Hospital administrative and pharmacy databases were queried for all short stay unit encounters at Lucile Packard Children's Hospital at Stanford University linked to infliximab infusions for IBD between January 1, 2006 to December 31, 2011. Descriptive statistics were used to generate comparative plots for drug and non-drug costs associated with CD and UC stratified by insurance type.
RESULTS: A total of 781 unique encounters were generated for 76 pediatric patients (47 CD, 29 UC). Out of the total direct costs related to infliximab administrations for either CD or UC patients, 77.3% of the costs per encounter were related to non-drug costs, such as personnel salaries (nursing), facility operations, supplies, and laboratory costs. 22.7% of the total costs were related to the actual infliximab drug costs. Based on a 60/40 payor mix of managed care vs. government-subsidized insurance payors, 45.5% of the total reimbursements were applied to non-drug costs in CD; 35.1% in UC.

CONCLUSIONS: Outpatient non-drug costs represent a substantial proportion of the total cost of infliximab-related actual costs in pediatric IBD. Personnel costs represent the largest segment of the non-drug costs. The actual drug costs of infliximab represent a small proportion of the total costs.

231 SCHIZOPHRENIC SUBJECTS WITH ELEVATED LEVELS OF NEURONAL TISSUE TRANSGLUTAMINASE 6 AND ANTI-GLIADIN ANTIBODIES. Debby Santora¹, Somaera Choudhary¹, Patricia Gregory², William Eaton², Nicola Cascella³, Alessio Fasano¹, ¹Center for Celiac Research, University of Maryland, Baltimore, MD; ²Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; ³Department of Psychiatry, Johns Hopkins, Baltimore, MD

Background: Celiac disease is an immune-mediated reaction to gluten, which can present with less commonly associated neurologic and psychiatric symptoms. Evidence of a link between schizophrenia (SZ) and celiac disease dates back as far as 1961. A theory for this association presented by Dohan was that gluten serves as an environmental trigger in individuals predisposed to SZ. Aims: To evaluate if there is a difference in the prevalence of antibodies against neuronal transglutaminase (tTG)-6 in a randomized group of SZ subjects that are positive for AGA-IgA vs those negative for AGA-IgA. Methods: Neuronal anti-tTG6 antibodies were assayed in 249 SZ patients. The 249 SZ are all negative for tTG-IgA 2 and the subjects were divided into two groups. Group 1 (n= 142) were positive for the AGA-IgA and Group 2 (N= 107) were negative for AGA-IgA. Age, gender matched controls were used. Results: Of the Group 1 had 27 samples test strong positive for anti-tTG6 antibodies (prevalence 1:6 or 19%), while group 2 had 14 tested strong positive for anti-tTG6 antibodies (prevalence 1:8 or 13%). As compared to controls; strong positive anti-tTG-IgA 6 were found to have a prevalence of 1:16 or 6%. Conclusion: Our preliminary observations suggest that the presence of neuronal anti-tTG6 antibodies in SZ patients are 2 folds higher in AGA-IgA negative subjects and 3 folds higher in AGA-IgA positive subjects, as compared to controls. There is a statistically significant difference between the AGA-IgA negative subjects as compared to the AGA IgA positive: P value of < 0.033. There is also a highly statistically significant difference between the two groups, as whole vs the control group: P value of < 0.001. These results point to a possible role of tTG6 as a biomarker of gluten sensitivity among SZ patients.

232 ANTI-TNF THERAPY INDUCED PSORIASIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Mohini G. Patel, Amy Amin, Uma P. Phatak, Dinesh S. Pashankar, Pediatric Gastroenterology, Yale University, New Haven, CT

Objective: Anti-TNF therapy (ATT) is commonly used for inflammatory bowel disease (IBD) and psoriasis. Interestingly, some patients on ATT develop psoriasis. We review our experience of children with IBD who developed psoriasis on ATT.

Methods: We reviewed the medical records of 36 children with IBD receiving ATT, specifically looking for the presence of psoriasis. To assess for possible risk factors associated with the development of psoriasis, we evaluated various factors including type of IBD, gender, age at diagnosis of IBD, presence of extraintestinal manifestations, and the number of doses and duration of ATT.

Results: Of the 36 patients receiving ATT, 6 patients (17%) developed psoriasis. Five were on infliximab (14%) and one (3%) was on adalimumab. Psoriatic lesions were on the face and scalp in 5 patients (83%), and the hands, chest, and legs in 1 patient (17%). Four patients had skin biopsies consistent with psoriasis. Psoriasis responded well to topical steroids and ATT was continued in all patients. Development of psoriasis did not affect the course of IBD. The table shows various factors between children with and without psoriasis. Only the presence of extraintestinal manifestation was significantly different between the two groups (p <0.01). Arthropathy was the most common extraintestinal manifestation.

Conclusions: Children with IBD can develop psoriasis on anti-TNF therapy. Psoriasis responded to topical therapy. The presence of extraintestinal manifestations, particularly arthropathy, was associated with the development of psoriasis.
<table>
<thead>
<tr>
<th></th>
<th>Psoriasis (n=6)</th>
<th>No Psoriasis (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn's disease</td>
<td>4 (67%)</td>
<td>20 (67%)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (67%)</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Age at IBD Diagnosis (years)</td>
<td>13.1</td>
<td>12.3</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>5 (83%)*</td>
<td>5 (17%)</td>
</tr>
<tr>
<td>ATT doses (mean)</td>
<td>6.4</td>
<td>14.3</td>
</tr>
<tr>
<td>ATT duration (months)</td>
<td>13.3</td>
<td>20</td>
</tr>
</tbody>
</table>

* P <0.01

**233 CAN C REACTIVE PROTEIN BE USED TO PREDICT SUCCESSFUL RESPONSE TO INFliximab IN PEDIATRIC CROHN DISEASE: RETROSPECTIVE STUDY.** Ashraf Alsahafi1,2, Mathew Carroll1, Mohammed Hasosah2, Kevan Jacobson1, 1Pediatric Gastroenterology division, UBC, Vancouver, BC, Canada; 2Department of Pediatric Gastroenterology, King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia

ESR and CRP are commonly used in the assessment of inflammatory activity in patients with Inflammatory Bowel Disease.

Aim of the study was to: 1) Evaluate the temporal relationship between CRP and disease activity (PCDAI) in pediatric patients with Crohn disease on infliximab treatment, 2) Determine whether the CRP level at commencement of infliximab can predict response to infliximab and 3) Correlate CRP measurements to other markers of inflammation, including ESR and monocyte counts.

Methods: Patient data was retrospectively collected from the established British Columbia Children's Hospital (BCCCH) Pediatric Gastroenterology Division IBD Database. Crohn's disease patients who received infliximab induction and maintenance for at least 30 weeks were included. Baseline variables and selected inflammatory markers (CRP, ESR, and monocyte count) were collected and evaluated. Results: From January 2002 to February 2012, 50 Crohn's disease patients fulfilled the inclusion criteria. The mean age of diagnosis was 11.3, and mean PCDAI was 36.5. The majority of patients had ileocolonic (n=13) or ileocolonic plus other small bowel disease (n=29). The remaining patients had isolated colonic disease (n=4) or colonic plus small bowel disease other than terminal ileal disease (n=4). Median disease duration to first infliximab infusion was 1.68 years. The CRP was most responsive with a decline observed in 70% of patients with high CRP following initial induction infusion. The CRP normalized in 82.1% patients post induction infusions with all 28 patients demonstrating clinical remission at week 30 . In contrast, symptoms and ESR declined more slowly resulting in a significant correlation for ESR with PCDAI after induction phase. No difference was observed between pre-infusion high (≥ 5 mg/L) and low (< 5 mg/L) CRP groups and their respective PCDAI score at week 30 (P = 0.84). Conclusion: In Crohn's disease patients on infliximab an early biological response was seen with a decline in CRP that preceded a significant decrease in ESR and PCDAI. A poor correlation between CRP, ESR and PCDAI was likely due to the slow more variable decline in ESR and PCDAI.

**234 CHILDREN WITH CROHN'S DISEASE ON 100% VS. 80% ENTERAL NUTRITIONAL THERAPY: INTERIM ANALYSIS OF A PROSPECTIVE COHORT STUDY.** Monica Lorusso1,4, Dale Lee1, Andrew Klink1, Kernika Gupta1, Ashley Martin1, Erin Gilroy5, Lisa Nessel1, Anthony Otley1, Anne Griffiths1, Paolo Lionetti4, Frederic Bushman3, Gary Wu3, James Lewis4, Robert N. Baldassano1, 1Children's Hospital of Philadelphia, Philadelphia, PA; 2Dalhousie University, Halifax, NS, Canada; 3University of Toronto, Toronto, ON, Canada; 4Meyer Children's Hospital, Florence, Italy; 5University of Pennsylvania, Philadelphia, PA

Background: The protocol for treating pediatric Crohn's disease (CD) with enteral nutritional therapy (ENT), recommendations for the avoidance of regular foods, and concurrent steroid use are widely varied. Therapy efficacy can be assessed both clinically and with fecal calprotectin (FCP) which correlates with mucosal healing.

Methods: Thirty children with active CD were initiated on ENT providing either 100% (15 Italian, 6 Canadian) or 80% (9 US) of estimated caloric needs. PCDAI and FCP were evaluated at initiation and after 8 weeks. The 100% group received a polymeric formula (Modulen, Osmolite) while 80% ENT received a semi-elemental formula (Peptamen Jr) plus ad lib food. Steroid exposure was followed. Paired and unpaired t-tests were used to assess differences within and between treatment groups.

Results: The 100% and 80% groups had similar demographics and initial disease characteristics. The majority of the 80% group was exposed to steroids (7 of 9 children), while the 100% group had no exposure over 8 weeks. The
mean decrease in FCP was 533 (p= 0.001) for 100% ENT and 281 (p= 0.23) for 80% ENT. Sub-analysis of the 80% group on no steroids or a stable dose for at least 14 days prior to ENT (n=5) showed a mean FCP decline of 658 (p=0.01). The 80% group (n=4) started on steroids concurrent to ENT had a mean increase in FCP of 348 (p=0.19).

Conclusion: Children on 100% and 80% ENT had significant decreases in PCDAI over 8 weeks. The 100% group vs. 80% group on no steroids or a stable dose had similar decreases in FCP.

235 THE ORAL MICROBIOME IN PEDIATRIC CROHN DISEASE. Judith R. Kelsen¹, Leah Posivak¹, Stephanie Grunberg², Aubrey Bailey², Robert N. Baldassano¹, James Lewis³, Frederic Bushman², Gary Wu¹
¹GI, Children's Hospital of Philadelphia, Philadelphia, PA; ²Biochemistry and Biophysics and Microbiology, The Hospital of The University of Pennsylvania, Philadelphia, PA; ³GI, The Hospital of the University of Pennsylvania, Philadelphia, PA

Background: IBD is associated with a dysbiotic gut flora. As oral manifestations are commonly found in Crohn disease (CD), we hypothesized that the oral microbiome may also be dysbiotic in patients with IBD. We characterized the subgingival oral microbiota in a longitudinal cohort of pediatric patients with CD and healthy controls to determine association with disease activity.

Methods: Subgingival plaque samples were obtained longitudinally from patients with CD and healthy controls at 2 time points. Samples were analyzed by 16S rDNA 454 sequencing. Clinical records and diet inventories were obtained. Disease activity was measured by Pediatric Crohn Disease Activity Index (PCDAI) and fecal calprotectin (FCP).

Results: 13 patients with CD and 13 controls were included. 85% of patients with CD demonstrated a decrease in PCDAI from severe disease, mean 37.5, to mild or quiescent disease at week 8, mean 13. There was a 77% decrease in the FCP from a mean 819, to a mean 401 at week 8. Using UniFrac to analyze microbial community composition, we found that the CD and control groups clustered separately at the second time point (p<0.001), and the CD cohort changed more between the 2 time points than the controls (p<0.001). These alterations were observed in the absence of clinical gingivitis.

Conclusion: This is the first study to demonstrate significant alterations in the subgingival oral microbiome in the absence of clinical gingivitis. Distinct clustering of the cohorts with decreased disease activity in patients with CD may indicate shifting states of the microbiome prior to settling into a new state. Additional analyses are underway to identify the taxa responsible for this finding. Newly diagnosed patients are being recruited to determine disease effect on the oral and gut microbiome.

236 PULMONARY NOCARDIOSIS - A RARE AND SERIOUS COMPLICATION OF TNF ALFA BLOCKERS IN CHILDREN. Arieda Gjikopulli, Ritu Walia, Joseph Wiley, Kalpana Murthy, Susan Lipton, Deepa Dutta, David Tuchman, Pediatric Gastroenterology, The Herman and Walter Samuelson's Children's Hospital, Baltimore, MD

Nocardiosis is a rare and serious complication of treatment with tumor necrosis factor alpha blockers. We present a case of pulmonary infection by Nocardia pseudobrasiliensis associated with infliximab treatment for Crohn's disease in an adolescent. A sixteen year old male patient with a history of Crohn's disease treated with 6-mercaptopurine, infliximab, and prednisone presented with a two-week history of fever, productive cough, dyspnea, chest pain, anorexia and weight loss. Chest X-ray revealed a 2 x 2 cm pulmonary nodule in the left anterior upper lobe. CT scan of the chest confirmed the presence of the nodule in the left anterior upper lobe, abutting the left carotid and subclavian arteries with a central area of necrosis. Routine blood and sputum cultures with stains for acid-fast bacilli were negative. Percutaneous biopsy of the nodule demonstrated necrotic material with questionable hyphae. Gram stain of the specimen was negative. Due to insufficient specimen, fungal and mycobacterial cultures were not sent. The patient was treated with caspofungin and amphophoricin B but remained febrile. Repeat chest CT demonstrated an increase in the size of the nodule with a central area of necrosis. Wedge resection of the lesion was performed and the specimen was sent for fungal, mycobacterial, bacterial cultures and PCR for Aspergillus, histoplasmosis, and blastomycosis. Nocardia pseudobrasiliensis was identified on fungal culture. The patient was started on high-dose trimethoprim/sulfamethoxazole. Immunosuppressive therapy was discontinued. His gastrointestinal symptoms were managed by bowel rest and total parental nutrition. The patient remained asymptomatic following treatment, with complete resolution of the nodule on a follow up CT scan. This case illustrates the diagnostic and therapeutic challenges faced in patients with inflammatory bowel disease infected with opportunistic organisms. Early recognition and treatment are necessary for prevention of disseminated disease and favorable outcomes.
237 AN OXYGEN EQUILIBRIUM AT THE HOST-MICROBIAL INTERFACE DETERMINED BY PHOSPHORESCENT NANOPROBE TECHNOLOGY. Colleen P. Judge1, L. G. Albenberg1, T. Esipova2, S. Grunberg2, J. Chen1, H. Li2, R. N. Baldassano1, J. D. Lewis2, F. D. Bushman2, S. A. Vinogradov2, G. D. Wu6
1The Children's Hospital of Philadelphia, Philadelphia, PA; 2The University of Pennsylvania, Philadelphia, PA
Background: The colonic lumen is largely devoid of oxygen and most gut microbes are obligate anaerobes. However, currently available technology is unable to quantify oxygen in the intestinal tract. Such measurements are essential to elucidate the host's relationship with its intestinal microbiota and may be relevant to human intestinal diseases such as inflammatory bowel disease.
Methods: Oxygen-sensitive phosphorescent nanoprobe Oxyphor G4 was administered to mice either orally or intravascularly to quantify intestinal luminal content or tissue oxygenation, respectively. A fiber-optic time domain phosphorometer was used to excite G4 and detect phosphorescence. Laparotomy was performed under isoflurane anesthesia and the decay pattern of G4 phosphorescence was measured in various organs. 100% oxygen was delivered to examine the effect of host oxygenation on luminal oxygen content.
Results: IV injection of G4 led to signal detection in all tissues, but ingested G4 was only detected at intestinal segments containing feces. The partial pressure of oxygen (pO2) was markedly lower in the cecal feces than in adjacent tissue. Inspiration of pure O2 led to a rapid, dramatic increase in cecal tissue pO2 and a delayed, gradual, more modest increase in luminal pO2. Both effects were reversible upon return to room air.
Conclusions: Our findings suggest that the anaerobic nature of the intestinal lumen is maintained by a dynamic equilibrium. We hypothesize that oxygen from colonic tissue is consumed by the gut microbiota, thus creating an anaerobic luminal environment. This concept is supported by our data in humans indicating enrichment of aerotolerant bacteria adherent to the rectal mucosa compared to the feces, where anaerobes predominate. Further optimization of this technique to quantify gut oxygen is underway.
238 withdrawn

239 PATIENT, PARENT AND PHYSICIAN AGREEMENT IN ASSESSING DISEASE ACTIVITY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Benjamin H. Shpeen, Emily Whitfield, Sally J. Eder, Emily M. Fredericks, Jeremy Adler, Pediatrics & Communicable Diseases, University of Michigan, Ann Arbor, MI
Background: Physicians, patients, and their parents often have different perspectives of disease activity in adolescents with inflammatory bowel disease (IBD). We set out to determine how often they concur in assessing active or inactive disease.
Methods: We recruited patients with IBD and their parents to each complete iPad surveys at their pediatric GI appointment. Physicians, blinded to surveys, also rated disease activity. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were recorded if available within one month of visit. Short pediatric Crohn's disease (CD) activity index (sPCDAI) and pediatric ulcerative colitis (UC) activity index (PUCAI) were calculated. Statistical analyses included κ statistic, χ2, and Spearman ranked sum.
Results: 69 patients (33 male) with CD (n=42; 10-19 yr) and UC or indeterminate colitis (n=27; 11-21 yr) were recruited. Disease duration ranged 2 mo-14 yr. Patients, parents, and physicians assessed disease activity as active or inactive. Parent-child agreement was 69.0% (κ= 0.33; p=0.006), parent-physician agreement was 75.0% (κ=0.45; p=0.0003), and child-physician agreement was 62.1% (κ=0.14; p=0.13). Child age and disease duration did not alter this agreement.
Parent agreement with the sPCDAI was poor (χ2=4.1; p=0.25) but approached significance for the PUCAI (χ2=1.0; p=0.075). Child's agreement was poor for sPCDAI (p=0.89) and PUCAI (p=0.83). Physicians agreed with sPCDAI (χ2=38.1; p=0.001) and PUCAI (χ2=28.8; p=0.001). Worse physician rated disease activity was associated with increased ESR (p=0.36; p=0.004) and CRP (p=0.25; p=0.0499).
Conclusions: It appears that patients with IBD have difficulty determining when their disease is active. Parents may be slightly better, but many still mistake their child's disease as active when inactive, or inactive when active. Physician assessment correlated with disease activity indices and lab evaluations. This study stresses the gap in perception of disease activity that may interfere with shared treatment decisions.
INTRODUCTION: About 1/3rd of hospitalized children with ulcerative colitis (UC) may have steroid-refractory disease. A 2011 international consensus states a Pediatric Ulcerative Colitis Activity Index (PUCAI) of 35-65 (moderate colitis) on day 5 warrants ongoing IV steroids and possible initiation of second-line therapy (calcineurin inhibitors or infliximab). A PUCAI >65 (severe colitis) on day 5 should prompt their initiation or colectomy. AIM: To examine patient outcomes after 5 days of IV steroids in accordance with the international framework.

METHODS: We reviewed standardized documentation (including daily PUCAI) from all admissions involving IV steroids for new or previously diagnosed UC from 7/1/2010-5/31/12. We excluded patients with colectomy, active infection, and Crohn's. Outcomes assessed included Day 5 PUCAI, length of stay (LOS), and initiation of second-line therapy. RESULTS: 69 patients with UC (median age 15 yrs (IQR 12, 17); 25 (36%) male) were admitted a total of 94 times for IV steroids during the study period. 55 (80%) had pan-colitis, and 22 (32%) were new diagnoses. Across admissions, median PUCAI was 60 (IQR 45, 65) on day 1; 35 (28, 55) on day 5; and 25 (15, 35) at discharge. Median LOS was 6 (IQR 4, 8) days and median IV steroid course was 4 (3, 6; range 2-28) days. 33% (31/94) admissions had a hospital stay < 5 days. Of 63 admissions ≥5 days, 9 had no PUCAI recorded on day 5, and 19 (30%) had a PUCAI 0-34. 3 patients (5% of admissions) had a PUCAI > 65 on day 5: 2 were started on second-line therapy and 1 underwent colectomy. Of 32 (51%) admissions with PUCAI 35-65 on day 5, 13 involved initiation of second-line therapy, with a median start date from admission of 5 days (IQR 2, 7; range 1-25); 1 admission involved >1 second-line therapeutic agent, and 6 led to colectomy. CONCLUSION: In >1/3rd of hospitalized children receiving IV steroids for UC, a PUCAI 35-65 was prospectively recorded on day 5. While using the recent international framework to manage severe UC appears reasonable, more guidance is needed regarding the management of this large proportion of patients with moderate colitis.

THE DEVELOPMENT OF A TRANSITION PROGRAM FOR ADOLESCENT/YOUNG ADULT PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Michele Herzer, Shawna Ricks, Brenda Starks, Hillary VanSlyke, Gastroenterology, Children's Mercy Hospitals and Clinics, Kansas City, MO

OBJECTIVES: Transition planning should be part of standard care for adolescents/young adults (A/YA) with IBD, yet few pediatric centers have standard practices for planning transition and transfer to adult care. Our aim was to develop transition guidelines to prepare A/YA with IBD to transition and transfer to adult providers.

METHODS: Transition guidelines were developed for a Midwest pediatric medical center. These were modeled after practice guidelines published by the American Academy of Pediatrics and by NASPGHAN. Fourteen on-site pediatric IBD medical providers provided commentary on the guidelines. These pediatric providers also provided feedback on a survey mailed to 100 local adult GI providers, designed to evaluate adult providers' experience in caring for young adults with IBD.

RESULTS: Transition guidelines were developed for IBD patients, ages 12 and older. Guidelines are developed as follows: Phase one (ages 12-14; sharing treatment responsibility between caregiver and patient, assessing disease/treatment knowledge), Phase Two (ages 15-17; continuing transition with increased responsibility by patient, initiating education regarding transfer), and Phase Three (ages 18-19; independent disease management by patient, completion of transfer). Pediatric provider feedback highlighted key topics to discuss with all patients (e.g., medication side effects, adherence, disease/treatment knowledge) and a need to identify community adult GI providers to transfer patients to. Among adult GI providers who completed the survey (29%), most had experience/training in IBD, one-fourth reported that 25-50% of their patient population was ages 18-25, and most would see patients before age 18.

CONCLUSIONS: An interdisciplinary approach that includes pediatric and adult GI providers in the development of transition guidelines is a promising program development approach. This is likely to facilitate co-management of patient care and ensure the transition-transfer needs of A/YA with IBD are appropriately met.

PRACTICE VARIATION IN THE TREATMENT OF IRON-DEFICIENCY ASSOCIATED WITH IBD. Sharad I. Wadhwani, Sabina Ali, Children's Hospital & Research Center Oakland, Oakland, CA

Anemia is a common problem in inflammatory bowel disorders (IBD). Specifically, iron deficiency anemia is frequently found and is thought to be multifactorial. These factors include chronic blood loss from inflamed bowel, dietary restriction and malabsorption. Treatment of iron deficiency anemia usually begins with oral iron, however, there is no clear stepwise approach to the treatment of anemia in pediatric IBD. The researchers surveyed major pediatric IBD centers to see if there were practice patterns for the treatment of anemia in IBD. Of the centers surveyed, 13 respondents from 10 institutions have responded to date. All centers report starting with oral iron as first line therapy. All but one respondent uses hemoglobin/hematocrit as a primary marker to initiate iron therapy. One respondent reported using serum iron levels less than 30 as an indication to begin iron therapy. Secondary markers of iron deficiency anemia were most commonly total iron binding capacity (TIBC), ferritin and mean...
corpuscular volume (MCV). There is significant variability in how frequently the response to treatment is assessed (Range: weekly to once every 3 months). Most respondents reported changing iron therapy to an intravenous formulation after they had determined treatment failure. However, there was significant variability in the initial type of intravenous preparation used with iron sucrose and iron dextran being the most frequently used formulations. One institution refers patients to hematology to initiate intravenous iron therapy. There is also great variability in the length of time patients are kept on oral iron before treatment failure is determined (1-6 months). The results capture variation in treatment practices for IBD associated iron deficiency anemia. From these results, we are able to create a protocol to treat this specific patient population. Further studies comparing the relative efficacy of oral iron to intravenous iron are needed to guide first line therapy and to establish best practices.

243 PSYCHOLOGICAL DISTRESS CORRELATES WITH DISEASE SEVERITY IN INFLAMMATORY BOWEL DISEASE. Colleen A. Nugent1, Peter S. Martin2, Chang-Xing Ma1, Robert D. Baker1, Susan S. Baker1, 1State University of New York at Buffalo, Buffalo, NY; 2University of Rochester, Rochester, NY
Adolescents who have IBD may experience psychological stress manifested as internalizing (depression, anxiety) and externalizing (somatic manifestations) symptoms. We hypothesize that disease severity in IBD correlates with psychological distress. A retrospective chart review was performed (from 10/1/10-10/1/11). There were 96 adolescents (mean age=15.13 years old, SD=2.94) diagnosed with IBD (%CD=68.42). Patients and their parents completed the Pediatric Symptom Checklist (PSC) and Youth Pediatric Symptom Checklist (YPSC) at each visit. We correlated those results with the Pediatric Crohn's Disease Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI). There was a strong correlation between parental and child scores on psychological factors (r=0.78, p<0.01). Total PCDAI scores correlated with overall PSC (r=0.23, p<0.01) and YPSC (r=0.20, p<0.01) scores, with correlations found for internalizing symptoms both on the PSC (r=0.37, p<0.01) and YPSC (r=0.30, p<0.01). PCDAI subscores for abdominal pain and patient function correlated with internalizing symptoms on the PSC (r=0.34, p<0.01) and YPSC (r=0.28, p<0.01). Total PUCAI scores did not correlate with overall PSC (r=0.26, p=0.06) or YPSC (r=0.34, p=0.02). There was a significant association between the total PUCAI score and internalizing symptoms per PSC (r=0.41, p<0.01). A significant number of PSC and YPSC screenings generated scores sufficient for mental health referral (17.98% and 12.22%, respectively). Overall IBD severity did correlate with overall psychological distress for CD but not for UC. Abdominal pain and level of patient function correlated with an increase in internalizing symptoms for CD. This tool offers insight into the psychological state of the adolescent, how psychological health is perceived by a parent and when an intervention by a mental health professional is indicated.

244 CONCORDANCE BETWEEN CHILD AND PARENT ASSESSMENTS OF QUALITY OF LIFE IN CHILDREN WITH IBD. Marina Orsi1, Gallo Julieta1, Sean Gauvry2, Albert Otley2, Ben McIntyre2, Carlos Lifschitz1, 1Hospital Italiano, Buenos Aires, Argentina; 2IWK Health Centre, Halifax, NS, Canada
OBJECTIVE: To compare the health-related quality of life (HRQOL) of pediatric patients with inflammatory bowel disease (IBD) assessed by themselves to that by one of their parents regarding major domains: bowel symptoms, emotional, social functioning, body image, systemic and treatment/interventions.
METHODS: The 35 item IMPACT III questionnaire was administered to IBD patients 9-17 yr old and one parent at the time of an outpatient visit. Demographic and disease-related information were prospectively obtained. The agreement between child and parent was examined by mean difference testing of IMPACT total and domain scores using paired t-test.
RESULTS: Seventeen ulcerative colitis (UC), 9 Crohn's disease (CD) and 1 indeterminate colitis with mean age 14.2±3 yrs, 16 (60%) male participated. 17 (63%) were in remission; 7 (26%) had mild and 3 (11%) had moderate/severe disease activity. Mean child total IMPACT score was not significantly different compared with adult score (136.1±22.0 to 128.9 ±24.4, p=0.14). Except for systemic symptoms and social functioning domain, child mean scores were greater than parent scores. However, the only significant mean difference testing was found for the emotional domain, where parents significantly underestimated the emotional functioning of their child (-3.4±5.4, p=0.003). CONCLUSION: In this population with most patients in remission, there was great concordance of HRQOL responses between patients and parents. However, this was not the case with emotional domain items of the IMPACT questionnaire. While parents may reliably give assessments of their child's HRQOL, the may underestimate their emotional functioning.
245 REFERRAL PATTERNS AND FOLLOW-UP FOR CHILDREN WITH ULCERATIVE COLITIS AT A SINGLE TERTIARY CENTER. Keith Breglio, Clare Ceballos, Nanci Pittman, Kathy Hoffstadter-Thal, Ruijun Bao, Keith Benkov, Children's IBD Center, Division of Pediatric Gastroenterology, Mount Sinai Medical Center, New York, NY

There are poorly established standards of care for treatment of IBD and consequently much variability between treatment centers. Retrospective studies can be useful in determining outcomes in many diseases, including ulcerative colitis (UC). Determining optimal treatment strategies based on patient outcomes is complicated by poor continuity of care in patients who move between providers.

Aims: Determine the origination of a group of pediatric UC pts at a single tertiary center & subsequent follow-up.

Methods: The Mount Sinai Children's IBD Center database started on 1/1/95 was used to identify children with UC. Determination was made whether the child was newly diagnosed and hence native to the institution, or whether they had been diagnosed at another institution and were coming for a 2nd opinion. Native pts & those 2nd opinions who stayed for ongoing care were designated as active, aged out or left the Center.

Results: Of 1827 records of children with IBD, 585 UC pts were identified. The mean age of diagnosis was 10.7 +/- 4.5 yrs & 326 were male. Of the total UC subjects, just over 2/3 or 402 patients were seen as 2nd opinions & approximately 1/2 (203) were seen for only one visit. The remaining 199 pts stayed for ongoing care with roughly 1/4 (55) leaving for other centers yet again, & the remaining 144 either remaining active or aging out. Of the 183 subjects who were diagnosed natively, the average age was very similar at 11.0 +/- 4.8 yrs and 102 were male. Of these subjects, 3/4 or 135 stayed for ongoing care and remain active or aged out, while 48 left prior to age 18 yrs.

Discussion: At our center, roughly 1/3 of all UC pts are diagnosed natively. The remainder are diagnosed at other centers, half of whom come for a single visit and half who stay for ongoing care. Interestingly, of 2nd opinions staying for ongoing care, 1/4 eventually leave for still other centers. Patients appear to be very fluid in where they obtain their care adding to the difficulty of establishing outcome based treatment guidelines. Similarly, studies of outcome, may be very influenced by the type of patients included.

246 ETHNIC COMPARISONS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN SOUTHERN NEVADA. Rebecca Scherr1, Howard Baron1, David Gremse2, 1University of Nevada School of Medicine, Las Vegas, NV; 2University of South Alabama, Mobile, AL

Objectives: Inflammatory bowel disease (IBD) affects all ethnicities. Most of the published epidemiologic data is from Caucasians and little is published about IBD in Hispanics. Our aim is to compare IBD among ethnicities in the pediatric population of Southern Nevada, which has a significant Hispanic population. Methods: This is a retrospective study of patients with ulcerative colitis (UC), Crohn's disease (CD) or indeterminate colitis (IC) seen at 2 large pediatric gastroenterology clinics in Las Vegas between 2004 and 2011. Type and extent of IBD, gender, age at diagnosis, medications and ethnicity were recorded. Ethnicity was defined as African American-non Hispanic, Caucasian- non Hispanic, Hispanic, Asian, and unknown. Logistic regression analyses were conducted to ascertain whether the prevalence of CD, IC, or UC varied significantly as a function of ethnicity. One-way ANOVA was conducted to ascertain whether age at diagnosis, exposure to biologics or presence of pancolitis differed between ethnicities. Results: Participants included 147 children. Ages ranged from 2.5 to 18 years (M=11.63, SD=3.90). There were 76 (51.7%) females. Five patients (3.4%) were diagnosed with IC, 56 (38.1%) with UC, and 86 (58.5%) with CD. Thirteen patients (8.8%) were African American, 98 (66.7%) were Caucasian, 29 (19.7%) were Hispanic, and 7 (4.7%) were unknown/other. African Americans and Caucasians were more likely to be diagnosed with CD than Hispanics by approximately 77% and 12%, respectively. The incidence of pancolitis was not statistically different among ethnicities. However, Hispanics and Caucasians were more likely to be exposed to biologics than African Americans by 25% and 22%, respectively. Caucasians were diagnosed at an earlier age (M=11.43, SD=3.88) than African Americans (M=13.23, SD=3.21). Conclusion: Our findings suggest that African Americans and Caucasians are more likely than Hispanics to be diagnosed with CD, but Caucasians are younger at diagnosis. Also, Caucasians and Hispanics have higher exposure to biologics than African American patients.

247 ASSESSMENT OF TRANSITION READINESS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Emily Whitfield, Benjamin H. Shpeen, Sally J. Eder, Emily M. Fredericks, Jeremy Adler, University of Michigan, Ann Arbor, MI

Background: Transition from pediatric to adult care may be associated with poor health. Checklists for transition readiness of adolescents with inflammatory bowel disease (IBD) developed by NASPGHAN and ImproveCareNow have not been well studied. Our goal was to test these checklists and establish baseline knowledge of transition readiness. We hypothesize that readiness will be associated with age and disease duration.

Methods: We recruited patients aged 10-21yr with IBD and a parent/guardian. Survey on iPad asked patient/parent to rate the patient's ability to perform tasks on 3-point scale (1=cannot do/needs a lot of help, 2=needs some help, 3=can do with no help). Task categories included: basic knowledge of IBD, independence at doctor visits, knowledge of medications, and IBD management. Associations with age and disease duration were tested with Spearman rank correlation.
Results: 67 patients (31 male) with Crohn disease (n=40), ulcerative colitis (n=25), and indeterminate colitis (n=2) and parent/guardians participated. Mean patient age was 15.7±2.5yr, and median disease duration was 5yr (2mo-14yr). Proportion of patients who reported ability to complete a task without help increased with age for: telling others their diagnosis (p=0.43, p=0.003), telling medical staff they do not like a treatment or are having trouble following it (p=0.37, p=0.003), and naming their medications (p=0.28, p=0.020). These did not vary with disease duration (p=0.26; p=0.72; p=0.53 respectively). Parent rating increased with child age for ability to name medications (p=0.32, p=0.013), but not to tell others their diagnosis (p=0.34). Neither varied with disease duration (p=0.56; p=0.31). Ability to identify flare improved with age per patient (p=0.32, p=0.009) and parent (p=0.26, p=0.048), but not with disease duration (p=0.77; p=0.54). Ability to get medications when ready did not vary with age (p=0.061; p=0.11), or disease duration (p=0.19; p=0.059).

Conclusions: Patients' ability to perform some key tasks of transition appears to improve with age, but not with disease duration.

248 POST-TRANSITION EXPERIENCE OF YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE. Jill M. Plevinsky, Janis Arnold, Laurie Fishman, GI/Nut., Boston Children's Hospital, Cambridge, MA

Background: and Aims The transition from a pediatric to an adult gastroenterologist for young patients with IBD is important for positive health outcomes. Physicians tend to report dissatisfaction with the preparation they offer their patients, or find their patients ill-prepared to become active agents in their health care (Hait et al., 2009). Also, older adolescents with IBD tend to report an incomplete understanding of their medications, and that their parents are largely responsible for their care. (Fishman et al., 2010). The objective of the present study is to evaluate the transition experience of young adult patients between age 25 and 30 who had been pediatric patients of the IBD Center at BCH.

Methods: A 25-item open response online survey was developed. Over 400 patients were invited to complete this survey regarding their transition experience. Preliminary responses were coded. Results: Themes include the importance of trust, communication between physicians, comfort, autonomy, and whether or not parents are present at pediatric and adult appointments. With a larger sample size, researchers will consider potential links between self-reported illness severity, age, and the previously identified codes. Findings will offer implications for program and policy development at BCH and institutions without transition curricula. Researchers suggest that policy and programming focus on enhancing communication between pediatric and adult practitioners, educating parents on the importance of a gradual transition, and preparing patients for the responsibility of their health care.


Concurrent Session II – Pancreas/Nutrition
Friday, October 19

259 IMPACT OF HIGH FAT DIETARY INTERVENTION ON RESTING ENERGY EXPENDITURE IN CHILDREN WITH CYSTIC FIBROSIS. Veronique Groleau1, Joan I. Schall1, Kelly A. Dougherty1,2, Norma E. Latham1, Asim Maqbool1,2, Maria R. Mascarenhas1,2, Virginia A. Stallings1,2, 1Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Pediatrics, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA

BACKGROUND: A lipid matrix (LYM-X-SORB™ [LYX]) has been shown to improve nutritional status in children with cystic fibrosis (CF) and pancreatic insufficiency (PI). Resting energy expenditure (REE), elevated in subjects with CF, may decrease as the nutritional status improves.

OBJECTIVE: To determine the effect of LYX vs. placebo with similar high fat and caloric content on REE and respiratory quotient (RQ) in children with CF and PI.

METHOD: Subjects (5 to 17 yrs) participated in a 12-month double-blind randomized supplementation trial of LYX vs. placebo. Both supplements had similar calorie and fat content, and LYX had higher choline. REE (kcal/d) was evaluated by indirect calorimetry at baseline, 3 and 12 months and % REE calculated using Schofield equations. Height (HAZ) and weight (WAZ) Z-scores were calculated and fat mass (FM) and fat free mass (FFM) assessed by DXA.

RESULTS: 63 children [57% males, age (mean±SD) 10.6±2.9] had REE measurements. Mean baseline % REE was 109±8% predicted. No difference in REE between the LYX (n=27) and placebo (n=36) groups was observed over time. In the total sample, REE (kcal/d) adjusted for FFM and FM significantly decreased at 12 months [(mean±SE) -32±12 kcals, p=0.009]. This decrease was significant in males (-49±16 kcals, p=0.002) but not in females (-8±19...
Growth status significantly improved [(mean±SD) -0.5±0.9 to -0.4±0.9 for HAZ, -0.4±0.7 to -0.3±0.8 for WAZ] and RQ significantly increased (0.86±0.07 to 0.90±0.06) over 12 months in both sexes on both LYX and placebo.

CONCLUSION: After 12 months of high fat supplementation, REE decreased in males and RQ increased in all children with CF and PI with concomitant improvement in growth status.

Supported by NIDDK(R44DK060302), Clinical Translational Research Center(UL1RR024134), Nutrition Center at Children's Hospital of Philadelphia, and Avanti Polar Lipids, Inc.


Biliary pancreatitis causes over 130,000 hospitalizations in the US each year. Reflux of bile into the pancreatic duct is thought to induce this form of pancreatitis. Bile acids cause pancreatic acinar cell injury via a sustained rise in cytosolic Ca2+. It is of clinical relevance to know the targets of this aberrant Ca2+ signal. We hypothesized that the Ca2+-activated phosphatase calcineurin (Cn) is such a Ca2+ target and that it mediates bile acid injury in isolated acinar cells and in vivo. To examine Cn activation, we infected mouse primary acinar cells with a luciferase reporter adenovirus, driven by the promoter for a downstream Cn effector NFAT. The bile acid tauro-lithocholic acid-3-sulfate (TLCS) was used to examine bile acid responses. TLCS caused Cn activation only at concentrations (500 uM) that cause acinar cell injury. The expression of Cn was unchanged over the 6 hr treatment time with TLCS. The activation of Cn by TLCS was abolished by chelating intra-cellular Ca2+ using BAPTA-AM or by inhibiting Ca2+ entry with the store-operated Ca2+ entry channel inhibitors BTP2 or SKF. Bile acids induced cell injury that could be tracked by LDH release and propidium iodide uptake. Pre-treatment with BAPTA-AM or the three specific Cn inhibitors FK506, CsA, or CiP prevented bile acid-induced acinar cell injury. The mechanism of cell injury appears to be through intra-acinar protease activation, since the Cn inhibitors reduced the activation of chymotrypsinogen within 30 minutes of TLCS administration by 52%, 87%, and 61%, down to control levels, respectively (n=3; P<0.05). In vivo, FK506 pretreatment reduced pancreatitis severity resulting from the retrograde injection of TLCS or tauro-cholic acid into the pancreatic duct of anesthetized mice by 66% and 93%, down to sham-treated control levels, respectively (n=5; P<0.05). Our data demonstrate that acinar cell Cn is activated in response to Ca2+ generated by bile acid exposure. Bile acid-induced pancreatic injury both in isolated acinar cells and in vivo is dependent on Cn activation. The findings suggest that Cn inhibitors may be an effective adjunctive therapy for biliary pancreatitis.

261 EVALUATION OF RESIDENT EDUCATION ON GI AND NUTRITION INPATIENT SERVICE. Amanda Muir, Lindsey Albenberg, Henry Lin, Children's Hospital of Philadelphia, Philadelphia, PA

Between resident responsibilities and the recent resident work hour restrictions, providing quality subspecialty medical education during resident rotations can be a challenge, specifically with regards to finding ideal timing and teaching methods. At CHOP, resident teaching during the pediatric GI and nutrition rotation occurs in the setting of a few structured didactic sessions and on rounds and the teaching of residents is highly variable. The aim of the study was to improve the quality of resident education during the pediatric GI and nutrition rotation. A survey was distributed to the 120 CHOP residents to assess their perceived importance of subspecialty education as well as the ideal timing and methodology for learning. Parallel surveys were distributed to 12 GI fellows. Respondents were asked to select pediatric GI and nutrition topics perceived as important to resident education. Of the 64 residents surveyed, they identified educational opportunities during residency as important and favored more directed learning either during rounds or through case studies. Residents find value in didactic sessions and prefer didactic teaching in the afternoon, as they felt that teaching on rounds interrupted the daily work flow. However, residents desired at least 1 hour of teaching, but receive less than 30 minutes. Of 12 fellows surveyed, they identified teaching residents as an important part of fellow education and would like at least 30 minutes of dedicated teaching time daily, but feel that they have less than 30 minutes a day. Fellows felt that teaching on rounds was the preferred teaching format. Pediatric residents identify a need for improved GI and nutrition education. Residents generally prefer to learn in the context of rounds, but feel that teaching on rounds hinders workflow and that afternoon teaching sessions provide a potential solution. Afternoon teaching sessions pose a challenge to the inpatient GI team. Finding a balance between productivity and teaching seems to be the major challenge facing resident education.
262 INCREASED PROCEDURE UTILIZATION AND COST IN OBESE AMERICAN CHILDREN.  
Nicole S. Steber¹, Nate A. Fleming¹, J. P. Molleston¹,³, Stephen M. Downs¹,², William E. Bennett¹,³  
¹Department of Pediatrics, IUSOM, Indianapolis, IN; ²Section of Children's Health Services Research, Indiana University School of Medicine, Indianapolis, IN; ³Section of Pediatric Gastroenterology, Hepatology, and Nutrition, Indiana University School of Medicine, Indianapolis, IN  
Objective: We performed a retrospective analysis of large-scale administrative data to determine the differential in procedure utilization and procedure-related cost in obese vs. nonobese children.  
Methods: Children from 2-21 years of age undergoing procedures in the PHIS database from 2004-2011 were included. The rate of procedures in children with an obesity-related ICD-9 code were compared to children without such codes using odds ratios, the Z-test for significance, and the Bonferroni correction. We computed the cost differential for patients with and without each procedure.  
Results: Over 3 million procedural encounters were included. T&A and internal femur fixation were more common in obese children in both settings. Inpatient procedures with higher rate included: CPAP, lap. cholecystectomy, physical therapy, and lumbar puncture. Ambulatory procedures with a higher rate: EGD, liver biopsy, colonoscopy, sigmoidoscopy, tibia/fibula implant removal, and pilonidal cyst excision. Procedures occurring at a lower rate: chemotherapy, lap. appendectomy, and PRBC transfusion in inpatients; myringotomy and crown application in outpatients. The average per-patient cost increase varied by procedure, ranging from $1,134 to $27,844.  
Conclusions: The presence of obesity-related ICD-9 codes in children is associated with increased rates of some procedures, as well as substantially increased costs.  

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Setting</th>
<th>N (Non-obese)</th>
<th>N (Obese)</th>
<th>Odds Ratio</th>
<th>Z test P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&amp;A</td>
<td>Outpatient</td>
<td>150235</td>
<td>4538</td>
<td>1.73</td>
<td>3.9x10^-64</td>
</tr>
<tr>
<td>EGD</td>
<td>Outpatient</td>
<td>155393</td>
<td>3723</td>
<td>1.37</td>
<td>1.0x10^-15</td>
</tr>
<tr>
<td>Closed Liver Biopsy</td>
<td>Outpatient</td>
<td>2356</td>
<td>428</td>
<td>10.4</td>
<td>1.9x10^-6</td>
</tr>
<tr>
<td>T&amp;A</td>
<td>Inpatient</td>
<td>7617</td>
<td>1609</td>
<td>6.66</td>
<td>8.2x10^-21</td>
</tr>
<tr>
<td>CPAP</td>
<td>Inpatient</td>
<td>18074</td>
<td>2000</td>
<td>3.49</td>
<td>9.2x10^-21</td>
</tr>
<tr>
<td>Lap. Chole</td>
<td>Inpatient</td>
<td>8403</td>
<td>1038</td>
<td>3.89</td>
<td>2.6x10^-7</td>
</tr>
</tbody>
</table>

Plenary Session II  
Saturday, October 20, 2012

Young Faculty Clinical Investigator Award

263 THE NATURAL HISTORY OF FIBROCYSTIC LIVER DISEASE IN PEDIATRIC ORGAN TRANSPLANT RECIPIENTS. Jessica Wen, Rebecca Ruebner, Bernard Kaplan, Susan Furth, The Children's Hospital of Philadelphia, Philadelphia, PA  
Introduction: Fibrocystic liver disease is a genetically heterogeneous developmental disorder that affects the liver and kidneys. Affected patients can develop portal hypertension, recurrent cholangitis and renal failure, requiring liver and/or kidney transplant. We report a cohort of pediatric transplant recipients in the U.S. with fibrocystic liver disease. Methods: Retrospective cohort study of pediatric (≤18 yrs) liver or kidney transplant recipients with diagnosis of polycystic kidney disease (PKD), congenital hepatic fibrosis, Caroli's disease, or nephronophthisis from 1/1990 to 3/2011 using data from the Scientific Registry of Transplant Recipients (SRTR). Subjects were categorized by the first transplanted organ; liver-alone (LT), kidney-alone (KT), or simultaneous liver-kidney (SLK). Subjects were excluded if they had a liver or kidney transplant prior to the start of the study period. Subjects were followed from the date of first transplant until death or end of follow-up. Mortality was ascertained through center reporting and supplemented with the Social Security Death Master File. Results: 716 subjects were included (73 LT, 602 KT, 41 SLK). Overall median age at time of first transplant was 9.7 yrs [IQR 3.6, 14.7]. During an overall median follow up of 8.5 yrs [4.7, 13.3], 81 (11%) subjects died (17 LT, 59 KT, 5 SLK). Of the 73 LT, 14 (19%) required a second liver transplant at a median of 0.2 yrs [0.01, 3.6] and 4 (5%) required a kidney transplant at a median of 8.0 yrs (6.0, 10.4) after liver transplant. Of the 602 KT, 116 (19%) required a second kidney transplant at a median of 7.7 yrs [3.3, 10.5]; 14 of these were SLK. 15 (2%) of KT subsequently received a liver transplant at a median of 4.6 yrs [3.4, 8.6]. Of the 41 SLK's, only 2 were re-transplanted (1 liver then kidney, 1 SLK). Conclusion: Pediatric patients with fibrocystic liver disease are more likely to receive kidney than liver transplants. The risk of subsequently needing transplantation of an alternate organ is low for both liver and kidney transplant recipients. Mortality for SLK is comparable to single organ transplants.
Young Faculty Investigator Award

264 PARAOXONASE GENE EXPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Razan H. Alkhouri, Susan S. Baker, Humaira Hashmi, Robert D. Baker, Wensheng Liu, Lixin Zhu, Digestive Disease and Nutrition Center, SUNY at Buffalo, Buffalo, NY

Background: The pathogenesis of Inflammatory Bowel Disease (IBD) remains unknown. The Paraoxonase (PON) 1, 2 and 3 genes are expressed in the human intestine and have a role in preventing oxidative stress and modulating inflammation. We investigated the impact of IBD and steroid therapy on the expression of PONs.

Methods: Patients included in the study were diagnosed with IBD. Age and sex matched control subjects were selected from those who had normal biopsies from endoscopy and colonoscopy. CaCo-2 cells were treated with H2O2 or dexamethasone for 24 hours; untreated cells served as control. PONs expression was evaluated by quantitative real-time PCR for both the biopsies and the Caco-2 cells. Results: PON gene expression was decreased in the biopsies from patients with IBD compared to controls (Table 1). PON gene expression in terminal ileum and sigmoid colon of IBD patients on steroids was increased compared to controls. H2O2 decreased PON gene expression in CaCo-2 cells (p <0.05). Dexamethasone increased gene expression of PON (p <0.05).

Conclusion: The expression of all PON genes is reduced in medication naïve patients. In vitro H2O2 decreases PON gene expression. The decrease in PON gene expression after an initial oxidative stress may play a role in the pathogenesis of IBD by further increasing oxidative stress induced damage at the mucosal level. In vivo and in vitro steroids can counteract the effect of oxidative stress in IBD by up regulating PON gene expression. Our study suggests a mechanism for the beneficial effect of steroids in the treatment of IBD. Interwoven in the pathways of oxidative stress, PON genes may be novel targets for the management of intestinal diseases like IBD.

<table>
<thead>
<tr>
<th></th>
<th>TI</th>
<th></th>
<th>SC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD compared to NC</td>
<td>UC compared to NC</td>
<td>CD compared to NC</td>
<td>UC compared to NC</td>
</tr>
<tr>
<td>PON 1</td>
<td>93%*</td>
<td>92%*</td>
<td>75%*</td>
<td>67%*</td>
</tr>
<tr>
<td>PON 2</td>
<td>87%*</td>
<td>85%*</td>
<td>85%*</td>
<td>86%*</td>
</tr>
<tr>
<td>PON 3</td>
<td>99%*</td>
<td>98%*</td>
<td>99%*</td>
<td>99%*</td>
</tr>
</tbody>
</table>

Table 1. Percent decrease in relative gene expression of PON genes in CD and UC when compared to NC. *p value < 0.05

Concurrent Session III – IBD and Intestinal Disorders II

NASPGHAN Endoscopy Prize

265 SINGLE CENTER EXPERIENCE OF ONE-STEP LOW PROFILE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE PLACEMENT IN CHILDREN. Nicole Pattamanuch, Inna Novak, Yolanda Rivas, Anthony Loizides, Andrea Montalvo, John Thompson, Debra Pan, The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, New York

Introduction: The use of one-step low profile percutaneous endoscopic gastrostomy (PEG) tube is a relatively new approach with limited data on complication rates and outcomes in the pediatric population. The one-step PEG has the benefit of utilizing a single procedure that immediately allows the family to use a low profile device. We report our experience with initial one-step PEG placement. Method: We performed a retrospective chart review of pediatric patients up to the age of 21, who had a one-step PEG placed by our pediatric gastroenterologists between 2006 and 2011. Patients were followed for a minimum of 6 months post-procedure. Results: A total of 146 patients underwent PEG placement; of these, 121 met follow-up criteria. Our population was comprised of 40% males and 60% females, with 23% under 12 months of age. The predominant indications for PEG were swallowing dysfunction and malnutrition. Many patients had multiple comorbidities, 30% had a history of prematurity. Post-PEG complications included granulation tissue 50% (61/121), cellulitis 21% (26/121), leakage 19% (23/121), broken device 11% (13/121), embedded bolster 5% (6/121), and gastro-colonic fistula 0.8% (1/121). The time for changing from one-step PEG to balloon gastrostomy tube (GT) ranged from less than one month to over 4 years (mean 14 months, N=65). Nine patients had PEG placed during PICU admission; two were lost to follow-up. Fifty-seven percent (4/7) no longer needed GT feeds by 4 months post-placement. Conclusion: The complication rate in our one-step PEG was comparable to that of standard PEGs, suggesting that the one-step procedure may be preferable for pediatric patients. The complication rate for local granulation formation may be higher than the standard PEG, which may highlight the importance of educating and training caretakers. Additionally, the critical care setting may not be the appropriate place to consider gastrostomy feeds.
266 INFLUENZA IMMUNIZATION IS NOT ASSOCIATED WITH ADVERSE EVENTS IN CHILDREN WITH IBD: A POPULATION-BASED STUDY. Eric I. Benchimol1,2, Steven Hawken2, Jeff Kwong2, Kumanan Wilson2, 1CHEO IBD Centre, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2Institute for Clinical Evaluative Sciences, Ottawa, ON, Canada

BACKGROUND: Influenza immunization is recommended for children with IBD, however case reports describe disease flares following vaccination. We assessed whether influenza vaccine was associated with adverse events in IBD patients using the Ontario Crohn's and Colitis Cohort.

METHODS: Using Ontario health administrative data, we identified flu vaccinations in all children diagnosed with IBD from 1999-2017, matching each IBD patient to 5 non-IBD controls by sex, age and region. We used a self-controlled case series (SCCS) model that assesses whether excess adverse events occurred in any 2-week risk period up to 180d post-immunization compared to a no-risk control period. The SCCS is a conditional Poisson model which compares each person to him/herself, thus controlling for fixed covariates. We calculated the relative incidence (RI) of health services (HS) use (hospitalizations, ER visits and outpatient visits) as a proxy for adverse events associated with influenza vaccination. RIs were compared between IBD cases and controls using relative incidence ratios (RIR).

RESULTS: 4916 IBD patients were matched to 21,686 controls. 25.3% of IBD patients and 13.2% of controls ever received immunization (P<0.001). In general, IBD cases had higher baseline rates of HS use than controls. In IBD cases, there were no significant HS use increases in risk periods compared to control periods adjusted for age and season (pooled RI 0.95, 95% CI 0.84-1.07), including hospitalizations (RI range 0.57-2.01) and ER visits (RI range 0.72-1.57). There was a slightly higher RI in IBD cases versus controls for days 3-14 (RIR 1.60, 95% CI 1.05-2.44, P=0.03). However from 15-180d, IBD cases had a lower RI compared to controls (pooled RIR 0.85, 95% CI 0.74-0.97, P=0.02).

CONCLUSION: There was no increase in HS use in the post-vaccine risk period in IBD patients, and the risk was comparable to healthy controls. Influenza immunization is safe in children with IBD and should be encouraged to improve poor coverage rates.

267 SUCCESSFUL MODIFIED DIETARY TREATMENT OF NON-RESPONSIVE CELIAC DISEASE: NOT ALL RESISTANCE TO A GLUTEN-FREE DIET IS REFRACTORY SPRUE. Justin Hollon1,2, Pamela Cureton2, Elaine Leonard Puppa2, Alessio Fasano2, 1Ped GI, Johns Hopkins, Baltimore, MD; 2Center for Celiac Research, UMD School of Med, Baltimore, MD

BACKGROUND: Patients with persistent symptoms or villous atrophy despite strict adherence to a gluten-free diet (GFD) have non-responsive celiac disease (NRCD). A subset of these patients has refractory sprue (RCD), requiring immunotherapy. Some NRCD patients may simply be sensitive to gluten cross-contamination in processed foods. Here we describe the effects on NRCD of a 3-6 month diet of exclusively naturally gluten-free foods, termed the "Fasano diet" (FD). We aim to demonstrate that, in addition to being an effective treatment for NRCD, this diet would reclassify the majority of patients thought to have RCD.

METHODS: We reviewed the records of all NRCD patients cared for in our celiac center, from 2005-2011, documented to have started the FD. NRCD was defined as villous atrophy or a persistence or relapse of symptoms despite being on a GFD for ≥ 12 months. NRCD patients met criteria for RCD if they had villous atrophy in addition to symptoms. Response to the FD was defined as being asymptomatic after the diet, with normal villous architecture on repeat biopsy, if performed.

RESULTS: 17 patients completed the FD; 15 were female (88%). Prior to the FD, all patients were interviewed by a celiac dietitian and no sources of hidden gluten ingestion were identified. Median age at start of the FD was 42 years (range 6-73); 5 patients were < 21 years of age. 14 patients (82%) responded to the FD; 3 underwent repeat endoscopy and all had complete healing of their celiac enteropathy. 6 patients met the criteria for RCD prior to the FD; 5 (83%) were asymptomatic after the FD and no longer met RCD criteria. Of the 14 patients who responded to the FD, 12 (86%) successfully returned to a traditional GFD without resurgence of symptoms.

CONCLUSION: The FD is an effective therapeutic option for NRCD patients that are not truly refractory. This diet spares them an inaccurate diagnosis of RCD and avoids immunotherapy. Most patients are able to return to a traditional GFD without return of symptoms.

268 A MAGNET AND BATTERY INGESTION EPIDEMIC? FOREIGN BODY INGESTIONS IN CHILDREN REPORTED TO THE NATIONAL ELECTRONIC INJURY SURVEILLANCE SYSTEM FROM 1997 TO 2010. Mazen I. Abbas1,2, Joon S. Choi2, Cade M. Nylund1, 1Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD; 2Pediatrics, Walter Reed NMMC, Bethesda, MD

Background: Foreign body ingestion (FBI) remains a public health problem in the United States and often requires emergency room care, endoscopy or surgery. In the past 10 years, there has been an increase in reports related to magnet and battery ingestions. We conducted an analysis of FBI and magnet ingestion in children utilizing the National Electronic Injury Surveillance System (NEISS). Methods: A retrospective, descriptive and trend analysis of FBI in children from 1997-2010. Data on FBI in children 0 to 17 years was obtained from NEISS, a web-based...
database (cpsc.gov). Data was also analyzed (available from 2002 to 2010) for the term "magnet". Projected estimates were calculated by using NEISS supplied variables. US Census Bureau (census.gov) age-based population estimates were used to determine incident rates. The Taylor series linearization method was utilized in calculating all national estimates and proportions confidence intervals. Trends were tested with the Cochrane-Armitage test. 

Results: The total national estimate of ER visits for FBI was 756,187 (95% CI: 634,450-877,922) with an incidence rate of 74 per 100K (95% CI: 62.1-85.9). Coins were the most commonly ingested objects (48%). Most visits resulted in no admission to a hospital (89.65%). However, multiple magnet ingestions as well as pin or needle ingestion had a high rate of admission. The number FBI visits increased from a rate of 57.1 per 100K (95% CI: 47.0-67.1) in 1997 to 95.4 (95% CI: 77.2-113.7) in 2010 (p<0.001). There was an increase in the ingestion rate of magnet ingestions from 2002 to 2010 (0.45 per 100K to 3.16) and batteries from 1997 to 2010 (1.4 per 100K to 5.6).

Conclusion: FBI remains a significant public health problem in the United States. There is an alarming increase in FBI especially magnet and battery ingestion in children. Preventative efforts need to continue to focus on public education and government regulations of hazardous objects to children.

Poster Session III
Saturday, October 20, 2012

Nutrition/Nutrition Support

269 INCREASING PREVALENCE OF OBESITY AT DIAGNOSIS OF CELIAC DISEASE IN CHILDREN.
Rebecca Abell, Kim Derespina, Anupama Chawla, Pediatric Gastroenterology, Stony Brook Children's Hospital, Stony Brook, NY, NY

Celiac disease (CD) can present with a variety of manifestations, especially in the pediatric population. Typically, children with CD are thought to be underweight, and suffering from abdominal pain and diarrhea. The current rate of obesity in children 2 to 19 years of age is 17%. Two recent studies have reported that 5-6% of children diagnosed with CD were obese (BMI >95%) at the time of diagnosis. Prior to these studies, there have only been case reports of obesity and CD in the pediatric population. Celiac disease is rarely considered in obese children with abdominal pain. This is a retrospective study of 96 pediatric patients diagnosed with CD between 2006 and 2012 at our institution. Data collected from the medical records included age, sex, weight, height, and BMI at time of diagnosis, presenting symptoms (including abdominal pain, diarrhea, and constipation), follow-up weight, height, and BMI one to two years after diagnosis. Patients were subdivided into underweight (UW), normal weight, overweight (OW), or obese, based on BMI percentiles. Five (5.2%) patients were UW, 65 (67.7%) were normal weight, 13 (13.5%) were OW, and 13 (13.5%) were obese. Obese and OW patients (42.3%) had a significantly higher rate of constipation compared to the normal weight patients (18.8%) as well as the general obese pediatric population (23%). Our study demonstrated an even higher prevalence of obesity at the time of diagnosis of CD than prior studies. In fact, our data demonstrates an incidence of obesity in celiac disease patients that is nearing the national prevalence. The incidence of constipation in this subgroup far surpassed the incidence in normal weight celiac patients and that reported in the general obese pediatric population, making celiac disease a likely contributor to the etiology of constipation. A significantly increased prevalence of obesity among newly diagnosed celiac patients as demonstrated in our study should encourage clinicians to screen obese children with abdominal pain, diarrhea and especially constipation for celiac disease.

270 PREVALENCE OF VITAMIN D INSUFFICIENCY IN SEVERE PEDIATRIC INFLAMMATORY BOWEL DISEASE.
Sophia Ali, Jonathan Moses, Sarah Worley, Naim Alkhouri, Pediatric Gastroenterology, Children's Hospital Cleveland Clinic, Cleveland, OH

BACKGROUND: Malabsorptive diseases, such as inflammatory bowel disease (IBD), place patients at higher risk for nutritional deficiencies including vitamin D insufficiency.

AIM: 1) To retrospectively assess the prevalence of vitamin D insufficiency in our population of pediatric patients severe IBD requiring infliximab treatment and 2) determine any significant relationship between vitamin D levels and clinical and demographic factors in our population.

METHODS: An IRB-approved retrospective chart review was performed. 100 charts were reviewed and patients included had undergone treatment with infliximab and had been treated for suboptimal vitamin D levels. Prior and post vitamin D levels were classified as > 30 sufficient, 16-30 insufficient, and < or = 15 deficient.

RESULTS: 100 charts were selected of patients with severe IBD on infliximab treatment, and 94 patients with IBD (8 with ulcerative colitis and 86 Crohn's disease) were included in the final results. Seventy-four percent of patients had insufficient vitamin D levels at first measurement, while 26% were insufficient at follow-up. Patients with non-caucasian race (P<0.001) and ileal-ileocecolic disease (P<0.04) were more likely to have suboptimal vitamin D levels. Patients with suboptimal vitamin D levels were more likely to be treated, and with higher dose vitamin D.
CONCLUSIONS: Vitamin D insufficiency is significant in our patient population with severe IBD, and these patients should be screened and treated with higher dose Vitamin D to improve their levels. Patients who are non-Caucasian in particular should have levels followed closely, along with patients who have ileal and ileocolonic disease.

271 EXCLUSIVE ENTERAL NUTRITION FOR PAEDIATRIC CROHN DISEASE- THE PATIENT AND CAREGIVER EXPERIENCE. Deirdre M. Burgess1, E. Notaras1, L. Heinsch1,2, E. Guest1,2, G. Woodhouse1, K. Marks1, D. Carmody1, C. Blumenthal1, S. Nightingale1,2, 1JHCH, Newcastle, NSW, Australia; 2University of Newcastle, Newcastle, NSW, Australia; 3Sydney Children’s Hospital Network- Westmead, Sydney, NSW, Australia Background: Exclusive Enteral Nutrition (EEN) is an effective yet underutilised therapy for the induction of remission in paediatric Crohn disease. We aimed to elicit patient and caregiver experience with EEN to determine factors that may influence uptake and compliance to therapy.

Methods: Separate focus groups involving patients and caregivers with experience of EEN were undertaken. Semi-structured open-ended questions were used to guide discussion and to elicit participants' experiences with EEN, the difficulties encountered, and suggestions to improve therapy provision. Transcript statements underwent thematic analysis achieving concept saturation and trustworthiness.

Results: Of 62 invited families, 16 patients (6 to 17 years) and 17 parents attended. Completion of >6 weeks of EEN using oral polymeric formula was achieved in 85% of participating patients. Seven major themes were identified: Sensory attributes including taste, temperature, volume, texture and satiety; Effectiveness of therapy; Practicalities such as cost, convenience, ease of use at school; Education provided prior to commencing, perceived attitudes of healthcare providers to EEN, experiences of other patients and families, internet resources, and the education of siblings, peers and schools around EEN; Support such as regular contact with medical team, parental and peer encouragement, access to support networks and to social workers and psychologists; Social and family impact including emotional reactions of child, impact on household routines, feelings of isolation and being different, impact on celebrations; Empowerment including patient/family involvement and autonomy in decision making to commence EEN.

Conclusions: Patient and caregiver experiences with EEN suggest a variety of themes which are likely to influence uptake of, and adherence to this therapy. Attention to these themes may allow for improved delivery and wider use of this effective therapy.

272 CHILD AND PARENT VARIABLES ASSOCIATED WITH THE USE OF ORAL NUTRITION SUPPLEMENTS. Douglas Field1, Helen M. Hendy2, Keith E. Williams1, 1Pediatrics, Penn State Hershey Childrens Hospital, Hershey, PA; 2Psychology, Penn State Schuylkill, Schuylkill Haven, PA

The present study provides the first examination of child and parent variables associated with use of nutritional supplements in children referred for feeding problems. Participants included 183 children and parents from a hospital-based feeding clinic (77 who do use supplements, 106 who do not; 70.5% boys; mean age = 71.6 months). Parents completed questionnaires with measures of oral motor and texture problems, the Child Eating Behavior Questionnaire, the Parent Mealtime Action Scale, and a food frequency measure of 85 common foods (fruits, vegetables, milk products, proteins, grain products, snack foods). Amount of supplement used daily was significantly explained (R² = .23) by children having lower weight, more oral motor problems, less Food Enjoyment, and (surprisingly) less Food Fussiness, and by parents using more permissive child feeding practices with Many Food Choices, and food consumption patterns of few Daily Fruits and Vegetables and many carbohydrate grain foods. One interpretation for present results would be that as parents use supplements to solve feeding problems experienced by children and themselves, they begin to perceive children as being "less fussy" during meals. Seeing these feeding problems as "solved" may lead to extended use of supplements, which could reduce children's opportunity to learn to eat a healthy variety of real foods. The goal of this study is to provide evidence-based recommendations pertaining to the use of oral supplements in children with feeding problems.

273 THE MODIFIED WHO PROTOCOL IN THE MANAGEMENT OF SEVERE ACUTE MALNUTRITION IN DEVELOPED COUNTRIES: A PILOT STUDY. Juliana Frem1,2, Craig Chu1, Christopher Swearingen1, Troy E. Gibbons1,2, George J. Fuchs1,2, 1University of Arkansas for Medical Sciences, Little Rock, AR; 2Arkansas Children's Hospital, Little Rock, AR

Introduction: The World Health Organization (WHO) protocol for the management of severe acute malnutrition (SAM) has resulted in a dramatic reduction in case fatality rates in developing countries. The conceptual approach of the WHO guidelines is relevant to the developed country setting, however would require significant modification. The protocol is underutilized in developed countries.

Methods: This is a retrospective case-control study of children (2months -6 years) with SAM (weight/length < - 3 SD) who received the modified WHO protocol versus a random nutritional intervention. Weight change models were adjusted for length of treatment and weight at initiation.

Results: 47 subjects were analyzed. 33% of the WHO group achieved a clinically meaningful outcome of a weight
increase of 10% during the hospital admission compared to 17% in the random group (p 0.89). Children receiving the WHO Protocol stayed in the hospital longer, had more phlebotomy draws, and had more electrolyte disturbances recorded (Table).

Conclusion: The WHO protocol achieved greater weight gain than random nutritional intervention; however the difference was not significant most likely because of type II error. The increase in length of stay, phlebotomy draws and electrolyte disturbances probably reflect increased awareness of and/or severity of malnutrition in the WHO group. These pilot results indicate expanded investigation is warranted.

### Weight and Outcomes by Treatment Group

<table>
<thead>
<tr>
<th></th>
<th>WHO Protocol</th>
<th>Random Intervention</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>24</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Weight Change(kg)</td>
<td>0.6 (0.9)</td>
<td>0.3 (0.2)</td>
<td>0.874</td>
</tr>
<tr>
<td>Percent Weight Change [N (%)]</td>
<td>5%</td>
<td>15 (62%)</td>
<td>15 (65%)</td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>8 (35%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Length of Stay (days)*</td>
<td>11.5 [4, 67]</td>
<td>6 [3, 29]</td>
<td>0.002</td>
</tr>
<tr>
<td>Phlebotomy Draws (N)*</td>
<td>8 [3, 56]</td>
<td>1.5 [0, 7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Electrolyte Disturbance [N (%)]</td>
<td>24 (100%)</td>
<td>13 (62%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Median [Min, Max] reported. Unless otherwise noted, Mean (Standard Deviation) reported.

274 LAPAROSCOPIC ASSISTED PEG TUBE INSERTION USING A LOW-PROFILE DEVICE-A MULTIDISCIPLINARY APPROACH. Carl-Christian Jackson¹, Tamara Feliciano-Alvarano¹, Peter D. Ngo², Walter J. Chwals³, Alejandro Flores³, ¹Pediatric Surgery, Floating Hospital for Children at Tufts Medical Center, Boston, MA; ²Pediatrics, Tufts University School of Medicine, Boston, MA; ³Pediatric Gastroenterology, Floating Hospital for Children at Tufts Medical Center, Boston, MA

**Background and Aims:** Percutaneous endoscopic gastrostomy (PEG) tubes have been used for many years to provide enteral access for adults and children. PEGs can be placed using only gastroscopy to guide percutaneous access of the stomach followed by antegrade passage of a long-stem G-tube, however this risks injury to the colon, liver and other organs. We use laparoscopy routinely to prevent such complications, and also to permit initial insertion of a low-profile device, which allows a safer and easier first exchange of the tube. The laparoendoscopic approach also guides tube placement on the stomach to minimize tension and avoid pyloric obstruction.

**Methods:** Retrospective review of laparoscopic-assisted percutaneous endoscopic gastrostomy with primary button placement (LAPEG-PBP) at a single institution from 2009-2012.

**Results:** 28 patients were included (43% female, age range 34 days-18 years, mean follow-up 11.8 months). All patients had feeding difficulties, with secondary diagnoses including traumatic brain injury, metabolic disease and chromosomal abnormalities. Preoperative nutrition included oral, NG, NJ and IV routes. Mean time to goal feeding was 2±1.1 days, and mean length of hospital stay for 22 non-neonatal patients was 3.7±3.5 days. Gastropexy sutures were removed on postoperative day 13± 3.9. There were no intraoperative complications. Postoperative complications included reflux (7 patients: resolution in 1, and 1 requiring fundoplication); 1 tube dislodgement in PACU requiring immediate return to the OR; gastropexy suture failure in 3; and surgical site infection in 6 (3 required systemic antibiotics; 3 resolved with suture removal).

**Conclusions:** LAPEG-PBP provides a safe means for insertion of a low-profile gastrostomy tube, preventing the need for later anesthesia and endoscopic exchange of the feeding tube. Goal feedings are rapidly achieved, with minimal post-operative complications.

275 NUTRITIONAL STATUS OF CHILDREN WITH INBORN ERRORS OF PROTEIN METABOLISM IN A PRIVATE NUTRITIONAL PRACTICE IN BOGOTA, COLOMBIA. Liliana Ladino¹, Erika Ochoa², Natalia Sepulveda¹, ¹Pontificia Universidad Javeriana, Bogotá D.C., Colombia; ²Instituto Tecnológico y de Estudios Superiores de Monterrey, Mexico DF, Mexico

Little is known about the nutritional consequences of inborn errors of metabolism (IEM) without neonatal diagnosis in Colombia. The aim of our study is to describe the nutritional characteristics of individuals with IEM who attended a nutritional private practice in Bogotá, Colombia, and to evaluate whether this status is consequence of the disease or other social or demographic variables.

The following is a descriptive observational study with a cross-sectional design, in which anthropometrical measurements were taken along with a diet analysis and the recollection of social and demographic variables. A simple of 22 individuals was gathered: 45% women, 36% infants, 59% resided in an urban area and 77% had a low socioeconomic status (SES). More than 40% had an adequate nutritional status and 45% suffered growth
retardation; no differences were found between gender, area of residence, SES nor age group. Nearly 90% had adequate treatment adherence, fulfilling their nutritional requirements according to age, disease and limiting amino acids. The only difference found in dietary intake was among age group, in which the intake per kg of weight lowered as the individuals got older. Finally, we concluded that the main nutritional outcome in patients with EIM is growth retardation and it can be attributed to the disease rather than other social or demographic variables.

276 INCREASED HEIGHT IN OBESE PRESCHOOLERS AND OBESE PREPUBERTAL CHILDREN.
Alfredo Larrosa-Haro1,2, Elizabeth Lizárraga-Corona1,2, Larissa Velazco-Ruiz1,2, Juan R. Vallarta-Robledo1,2, Clio Chávez-Palencia1,2, Laura L. Salazar-Preciado1,2, María E. Cámara-López1,2, Hugo E. Sepúlveda-Vázquez1,2, Ana K. Rodríguez-Anguiano1,2, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Unidad de Investigación en Epidemiología Clínica, Hospital de Especialidades CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

AIM: To compare the height of obese and healthy weight preschool and elementary school children.

SUBJECTS AND METHODS: Design: cross sectional. Sample: 642 children attending kindergarten and elementary school were selected randomly and grouped in one-year class intervals from 4 to 12. Variables: Weight and height. Study groups were healthy weight (n=454) and obesity (n=188) according to BMI/CDC criteria; children with low weight and overweight were discarded. Weight and height mean differences were analyzed with ANOVA in the total sample and with Student t for each class interval.

RESULTS: Height was significantly higher in the obese group from 5 through 10 years with a maximum mean difference of 6.9cm in the 10-year group. By twelve years there was no height difference between obese and healthy weight children. Weight mean difference increased from 2.2kg in the 4-year group to 23.6kg in the 11-year children. By twelve years the weight mean difference was 22.2kg.

DISCUSSION: Although this was not a longitudinal study, a clear-cut 6-year period (5 to 10 years) in which height was progressively higher in the obese children was identified, suggesting increased growth speed. This condition has been observed by other authors suggesting an association with insulin resistance and increased sensibility to growth hormone. However, it is not clear if these biochemical/hormonal events occurs before or after weight excessive gaining begins.

277 ENERGY INTAKE, DIETARY HABITS, PHYSICAL ACTIVITY AND ITS ASSOCIATION TO OBESITY IN ELEMENTARY SCHOOL CHILDREN.
Alfredo Larrosa-Haro1,3, Guillermo J. González-Pérez2, Edgar M. Vásquez-Garibay1, Enrique Romero-Velarde1, Clio Chávez-Palencia1,2, Laura L. Salazar-Preciado1,3, Ana K. Ramírez-Anguiano1,3, Elizabeth Lizárraga-Corona1,3, María E. Cámara-López1,3, Hugo Sepúlveda-Vázquez1,3, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Ciencias Sociales, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 3Unidad de Investigación en Epidemiología Clínica, Hospital de Especialidades CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

OBJECTIVE: To elaborate a predictive model of obesity in children focused in energy intake, dietary habits and physical activity.

SUBJECTS AND METHODS: Design: Case control. Setting: A low middle-class elementary school at Guadalajara Mexico, random sample of children 6-12 years-old, 100 subjects per group. Inclusion: Obese (cases) and healthy weight (controls), CDC classification. Independent variables: energy intake, dietary habits and physical activity. Statistics: chi square and logistic regression.

RESULTS: Socio-demographic variables (age, gender, parents' age education and employment, type of family and family income) showed no differences. Energy intake of obese children was higher. Dietary habits associated to obesity were <4 meals a day, afternoon snack away from home and lonely school lunch. Food frequency intake of obese children was higher for junk foods, sweetened beverages and fats. Physical activity variables associated to obesity were lower time of spontaneous activity and longer time dedicated to homework and watch TV. The logistic regression models included diet and physical activity variables.

CONCLUSIONS: The variable with the higher association strength to obesity was energy intake and it was mainly determined by high density foods. Variables related to the domains of physical activity had lower association strength. The best predictive model included energy intake, dietary habits and physical activity. However, the diversity of regression models and variable interactions reflect the complexity and multifactorial character of childhood obesity.
278 BIOELECTRICAL IMPEDANCE ANALYSIS TO EVALUATE ADIPOSITY IN PRESCHOOLERS: TECHNICAL DIFFICULTIES. Elizabeth Lizárraga-Corona, Alfredo Larrosa-Haro, Larissa Velasco-Ruiz, Juan R. Vallarta-Robledo, Edgar M. Vásquez-Garibay, Enrique Romero-Velarde, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

Aim: To report the technical difficulties of bioelectrical impedance analysis (BIA) in preschoolers.

Subjects and Methods: A cross-sectional pilot study to evaluate body fat percentage was performed in 25 children 3-5 years old attending a kindergarten. Adiposity was evaluated with BIA (Bodystat, Quadscan 4000) and body fat percentage (Slaughter's equation). Electrode location for BIA technique was the published for children and adolescents. Means and SD of body fat percentage were compared with electrodes located at different distance of the anatomical standard sites.

Results: When electrodes were located at the conventional anatomical sites (wrist and proximal phalanges of the right dorsal hand plus ankle and proximal phalanges of the right dorsal foot), measurements of the fat percentages were too high (33.3, SD 9.2), when compared with body fat percentages obtained with the Slaughter's equation (p=0.007). Repeated BIA measurements with electrodes located at variable distances between them lead to the observation that its location at 6cm in right hand and 16cm in the right foot (16.6, SD 11.9) was similar and without statistical difference (p= 0.785) with the Slaughter's values (15.5, SD 5.5) and the McCarthy's reference pattern.

Conclusion: Experience with BIA in preschoolers is scanty and currently this technique may not be considered as a gold standard to measure adiposity. Further studies are needed to clarify this issue.

279 EATING DISORDERS IN ADOLESCENTS IN BOGOTA: A STUDY USING THE CHILDREN'S VERSION OF THE EATING ATTITUDES TEST (CHEAT). Yudy Leon, Rafael Guerrero-Lozano, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Background: Eating disorders (ED) are mental disturbances related to food that share an intense preoccupation regarding weight, food and body shape. Its etiology is unknown but is believed to result from the interaction of genetic, biological, psychological and social factors. They are classified as anorexia, bulimia and non-specified ED. They may produce serious consequences for physical and mental health and are at present a topic of interest to the scientific community.

Objectives: To determine the frequency of risk of ED in adolescents in Bogotá using the survey The Children's version of the Eating Attitudes Test (ChEAT). To assess distortion of body image in those at risk.

Patients and Methods: In a cross-sectional observational study performed in ten schools in Bogota, 991 adolescents of both sexes and different socioeconomic strata, without predisposing medical conditions, were surveyed and asked to complete the items included in ChEAT. Children were also requested to mark one of Gardner's figures as their BMI and with those regarded themselves as "fat". Percentages were 12 and 0.5, respectively, in those found. Concordance between BMI and body image was poor (Kappa= 0.088). In children at risk, 16.2% with normal BMI and 1.2% with underweight regarded themselves as "fat". Percentages were 12 and 0.5, respectively, in those considered not at risk. Adolescents found to be at risk are currently being assessed.

Conclusion: Although considerable, the observed frequency of ED was lower than previously published in Colombia; however, it is within the range found in reports elsewhere. Expert interviewing and diagnosis is still necessary to confirm and classify cases. Distortion of body image is not rare.

280 CYPROHEPTADINE USAGE IN CHILDREN WITH POOR ORAL INTAKE AND A FEEDING DISORDER: A RETROSPECTIVE CHART REVIEW. Goldie Markowitz, Amy Dean, Jeanette Trella, Andrea Mattie, Sherri S. Cohen, Feeding & Swallowing Center, The Children's Hospital of Philadelphia, Philadelphia, PA

Introduction: Children with feeding disorders often have limited oral intake, poor appetite, and are at risk for weight loss and malnutrition. Medications are used to stimulate appetite in order to improve weight gain in select adult and pediatric populations with chronic illness. There are no clinical studies in children with poor appetite as part of a feeding disorder. The purpose of this study is to evaluate the prevalence of cyproheptadine in children who present with poor appetite, decreased oral intake, and slow weight gain, as a component of a feeding disorder. We will examine the prescribing trends to evaluate the effectiveness, safety, and tolerability of cyproheptadine as an adjunctive therapy.

Methods: An IRB approved retrospective medical chart review of children seen in a multidisciplinary feeding and swallowing center between the years of 2003 to 2007 was performed. Children were included with a feeding diagnosis and malnutrition as defined by an ICD9 code of failure to thrive, slow weight gain, or underweight. The clinical data included information on the use of cyproheptadine, and when used, the dose, duration, and whether there were any side effects. Additional data, when available, was collected on weight and ideal body weight at each visit to the feeding and swallowing center, while the patient was receiving cyproheptadine.

Results: Twenty-nine patients (mean age 4.2 years) with a feeding disorder had been treated with cyproheptadine. A prevalence rate of 8% was documented. The mean dose 0.19 mg/kg/day and there were no adverse events were reported.

E93
Conclusions: Although controlled trials are necessary, our data suggests that cyproheptadine is safe and easily tolerated as adjunctive treatment for children with malnutrition and an associated feeding disorder. Despite difficulty in interpreting the data, a modest weight gain was demonstrated. Further studies are needed to demonstrate whether weight gain is sustainable with other modalities to treat a child with a feeding disorder.

281 AVAILABILITY OF FINANCIAL SUPPORT SERVICES TO PATIENTS ON GLUTEN-FREE DIET. Bradley Pelley, Mohsin Rashid, Dalhousie University, Halifax, NS, Canada

BACKGROUND: The treatment of celiac disease and other gluten related disorders is strict, life-long adherence to a gluten-free (GF) diet. The GF diet poses several challenges one of which is increased cost. Since the GF diet has to be followed for life and more than one family member may be consuming it, the cost over time can be substantial. Lack of affordability may lead to non-compliance with the diet and increased risk of complications.

OBJECTIVE: To investigate what financial support services are available to patients with celiac disease on a GF diet in various countries. The understanding of the financial implications of GF diet will help develop strategies for easing the economic burden for patients.

METHODS: A web search of all international celiac support organizations was conducted. A survey was sent to the organizations with questions about their membership and type(s) of financial assistance available for patients on a GF diet in the respective countries.

RESULTS: In total, 58 celiac support organizations were identified with 40 in Europe and 7 in North America. Twenty three (40%) completed the survey. Number of members in organization ranged from 125 to 70,000. The majority indicated that gluten-free food is at least three times more expensive than regular food. Only half of the responding organizations reported some form of financial support available to patients. This support came from a variety of sources including fixed stipend, subsidized GF products and income tax credit. Degree of support varied significantly between countries. Most suggested that the governments should take a lead in offering financial support to those of a GF diet.

CONCLUSION: Availability of financial support for patients on a GF diet is limited to some countries. A collaborative approach by international celiac organizations needs to be developed to strategize and lobby the governments in easing the economic burden of GF diet.

282 RELATIONSHIP BETWEEN DURATION OF BREASTFEEDING AND INTELLIGENCE QUOTIENT IN CHILDREN AT 7 YEARS OF AGE. Jose Potosi, Rafael Guerrero-Lozano, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Objectives: To evaluate the association between duration of exclusive breastfeeding (EB) and intelligence level of children aged 7 through IQ. To look for possible relationships between IQ and total breastfeeding time (TB), as well as age of weaning, and initiation of infant formula (IF).

Methods: In a private school, in order to standardize education, socioeconomic status, and parental education, 200 surveys were sent to families of children aged 7. There were 64 responses. Eight children were excluded due to perinatal history. Consent was obtained in 39 cases. Respondents were asked about medical history and early feedings, specifically duration of EB, BT, age of weaning (CF) and infant formula initiation. Each child sat the General and Differential Aptitude Battery, intelligence test.

The data were handled in Excel and Stata 10.1.

Results: Out of 39 children who underwent the test, one who did not finish it, was excluded. The study group, 22 (58%) boys, was 7.02 ± 0.4 years of age, had been EB for 3.5 ± 2.3 months, had TB for 11.6 ± 9.6 months, had been weaned at 4.1 ± 2.1 months and received IF at 6.6 ± 6.4 months. Their IQ was 119.3 ± 12.2. Significant association was found between TB and IQ. The age of initiation of IF was positively associated with numeracy and attention items at 52 and 35.7%, respectively.

Conclusions: This study shows that the longer the breastfeeding, the higher IQ. Later introduction of milk formula is associated with better outcomes in numeracy and attention.

283 FETAL GROWTH RESTRICTION IN PRETERM NEWBORNS AND ITS ASSOCIATION TO SOCIO-DEMOGRAPHIC AND PATHOLOGIC FACTORS. David Rodríguez-Medina1,3, Erika Hurtado-López2,3, Alfredo Larrosa-Haro2,3, Edgar Vásquez-Garibay3, Rogelio Troyo-Sanroman1, 1División de Neonatología, UMAE Hospital de Ginecobstetricia, IMSS, Guadalajara, Mexico; 2Unidad de Investigación en Epidemiología Clínica, Hospital de Especialidades, IMSS, Guadalajara, Mexico; 3Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

AIM: To evaluate the association of socio-demographic and pathologic factors with fetal growth restriction (FGR) in preterm newborns.

PATIENTS AND METHODS: Design: Transversal. Setting: A neonatology referral department. Inclusion: Preterm newborns, aging 28-36 weeks. Independent variables: socio-demographic and pathologic factors. Dependent variable: FGR and normal weight for gestational age (NWGA), Jurado-García reference pattern was used to obtain Socio-demographic variables were investigated with an ad hoc questionnaire; pathological data were obtained from
the mother's and patient's clinical charts. Statistics: Chi square, OR and 95%CI.

RESULTS: 65 (69.9%) newborn had NWGA and 28 (30.1%) had FGR. Weight of newborns with NWGH was 1824g and with FGR 1535g (p=0.025). FGR was associated to: higher father's education (OR=3.2, CI=1.1-9.5), single mother (OR=4.2, CI=0.9-21.6), family size (OR=4.5, CI 1.5-13.7), multiple pregnancy (OR=3.3, CI=1.1-9.9), smoking (OR=6.9, CI=1.0-74.8) and number of siblings (OR=3.5, CI=1.0-5.4).

CONCLUSIONS: A number of risk factors associated to FGR were detected. However, other conditions identified by other authors associated to FGR were found in both study groups; this may underestimate its possible influence in the physiopathology of FGR. Studies of body composition in neonates are needed to assess the influence of mother's health to newborns.

284 CHOLESTASIS, MULTIPLE EPISODES OF PARENTERAL NUTRITION THERAPY AND RISK FOR MILK-PROTEIN INTOLERANCE IN PRETERM INFANTS. Timothy Sentongo, Ellen Newton, Purser Melanie, Dana Weinstein, Ranjana Gokhale, Stacy Kahn, Stefano Guandalini, Pediatrics, University of Chicago, Chicago, IL

Aim: This study examined the clinical events implicating milk-protein intolerance in infants who received parenteral nutrition (PN) support.

Methods: The clinical course of newborn infants who received PN therapy over a 12 month period was reviewed. The clinical and laboratory parameters assessed included gestation age, birth weight, duration and number of courses of PN therapy, prevalence of cholestasis (conjugated bilirubin >1.5 mg/dL) and need to change from breast milk or intact protein formula to a protein hydrolysate (PH) or crystalline amino acid (CAA) formula.

Results: 348 infants received PN, 264 (76%) were weaned off within 3 weeks, 51/348 (15%) developed clinical symptoms that necessitated multiple courses of PN, and 19/348 (5%) required change from breast milk or intact protein formula, to a PH or CAA formula. Comparison of the infants who received multiple courses of PN with those who required only a single course of PN showed (median; range): lower gestation 27 weeks (23 - 36) vs. 32 weeks (23 - 41), p<0.001; lower birth weight: 958 g (425 - 2675) vs. 1743 g (465 - 5110), p <0.001 and; greater likelihood for change to a PH or CAA formula: 27% vs. 2%, p <0.001. Among those who received one course of PN that lasted ≥3 weeks, the onset of cholestasis was associated with longer duration on PN and greater likelihood for change to a PH or CAA formula compared to those without cholestasis: 21% vs. 3%, p = 0.021.

Conclusion: In this group of infants who received nutrition support, onset of PN cholestasis and multiple courses of PN were associated with increased likelihood of milk-protein intolerance. Therefore, occurrence of these events in preterm infants should prompt early transition to a PH or CAA formula.

285* COMPARATIVE EFFICACY OF MATERNAL SKIMMED BREAST MILK AND ALTERNATIVE LOW-FAT FORMULA IN POST-SURGICAL CHYLOTHORAX. Shaija Shelby, James Hammel, Sheela Rangamani, Shelby Kutty, David Danford, Ruben E. Quiros-Tejeira, University of Nebraska, Children's Hospital and Medical Center, Omaha, NE

Background: Postsurgical chylothorax (PSC) is a known complication after cardiothoracic surgery. We sought to investigate the effectiveness of maternal skimmed breast milk (SBM) with medium chain triglyceride vs. alternate low fat (portagen) formula in the treatment of PSC in infants.

Methods: A single-center review of all infants who developed PSC (7/2006 to 9/2011) was performed. PSC diagnosis was based on clinical and biochemical pleural fluid analysis. Demographics including age, weight, cardiac diagnosis/surgery, and other comorbidities were collected. Serial data from identification to resolution of PSC including the type of feeding, duration and volume of chest tube output, laboratory results and alternative PSC treatments [thoracic duct ligation (TDL), pleurodesis, octreotide] were tabulated.

Results: Of 48 patients (pts), 30 were males, and mean weight (wt) was 3.3±1 kg (0.85-6.2). The cohort had high rates of single ventricle heart disease (n=12, 25%), prematurity (n=13, 27%), and chromosomal anomalies (n=12, 25%). SBM was used in 12 pts (25%), portagen in 21 (44%) and both in 15 (31%). Mean time for PSC resolution and chest tube removal in the entire cohort was 8.5 and 12 days. 7 pts (14%) required TDL, 1 each had chemical pleurodesis and octreotide. Six pts (13%) died before PSC resolution due to various complications, of which 2 had TDL. The SBM-only group took fewer days to resolve PSC and fewer days to tube removal; however total volume and daily rate of drainage normalized to body weight were not different between groups.

Conclusions: In this challenging group of pts with major comorbidities, sole SBM therapy showed a marginal advantage for PSC resolution compared with diets that included portagen solely or portagen with some SBM. SBM therapy did not show an association with worse outcomes or TDL.
### 286 BENEFICIAL EFFECTS OF ORAL REHYDRATION SOLUTION ON ORTHOSTATIC INOLERANCE.

**Deepali Tewari**1,2, Arun Aggarwal1,2, Zachary Messer2, Marvin S. Medow2,1, Julian M. Stewart2

1Pediatric Gastroenterology, New York Medical College, Valhalla, NY; 2Pediatrics, New York Medical College, Valhalla, NY

**Background and Aim:** OI can cause excessive upright heart rate (HR) and a decrease in blood pressure (BP), initiated by postural contraction of central blood volume (CBV) by translocation of blood from the upper to lower body. Intravenous isotonic saline (IVS) CBV expansion effectively reduces OI regardless of etiology; oral hydration fails to provide similar benefit.

ORS (glucose+sodium) efficiently rehydrates cholera patients, suggesting it can increase CBV. We propose that equal volumes of ORS or IVS can improve orthostatic tolerance by mitigating changes in HR and BP in fainting patients.

**Methods:** We studied subjects with OI (N=4), with 3 postural faints during the past year or Postural Orthostatic Tachycardia Syndrome, and healthy controls (N=4), and separately evaluated baseline (no treatment), IVS and ORS. Orthostasis using Lower Body Negative Pressure (LBNP) was applied sequentially at -15, -30, -40 mmHg for 5 min each, and -55 mmHg for one hour or until OI was elicited.

**Results:** While controls tolerated -55 mmHg, fainters could not. Controls became tachycardiac with decreased pressure (32.4% HR increase from baseline), but fainter's HR remained unchanged during LBNP. In fainters, IV saline and ORS resulted in heart rate increases at -40 mmHg, significantly greater (p <0.05) than baseline. In controls, mean arterial pressure (MAP) remained unchanged from baseline to -40 mmHg, but decreased significantly (43.7 %, p< 0.01) in fainters. Following IV saline in fainters, MAP fell significantly comparing baseline to -40 mmHg (76.5±7.2 vs 54.9±2.4, (p<0.05)). In contrast, ingestion of ORS by fainters prevented this decrease as MAP remained unchanged (78.1±9.2 vs. 75.5±5.5 mmHg, baseline vs. -40 mmHg).

**Conclusion:** This pilot study suggests ORS may be beneficial in decreasing orthostasis in fainters, possibly afforded by allowing appropriate increases in HR and BP maintenance, thereby avoiding syncope. ORS may be a practical, cost-effective alternative to IVS for OI management.

### 287* LOW-DOSE OMEGA-6 AND LOW-DOSE OMEGA-3 PARENTERAL LIPID THERAPIES: IMPACT ON LIVER DISEASE AND NUTRITIONAL OUTCOMES IN PIGLETS.

**Justine Turner**1, Jessica Josephson1, Patrick N. Nation1, Consolato Sergi1, Pamela Wizzard1, Diana Mager1, Ronald O. Ball1, Paul B. Pencharz2, Catherine J. Field1, Paul W. Wales1,1University of Alberta, Edmonton, AB, Canada; 2University of Toronto, Toronto, ON, Canada

**Introduction:** Low dose intravenous lipid therapy (ILT) has been suggested as beneficial treatment for neonatal parenteral nutrition associated liver disease (PNALD). Direct comparison between low dose omega-6 (n-6, soy based) and low dose omega-3 (n-3, fish oil based) ILT are not reported. We investigated low dose n-6, and n-3 ILT compared to standard high dose n-6 lipid therapy and to sow fed piglets.

**Methods:** Three groups of neonatal piglets, 2-5 days (1.83-2.58kg) underwent a jugular catheter insertion to allow for 14 days of isonitrogenous total parenteral nutrition (TPN) delivery. Group 1 (n= 6) received 5g/kg/d n-3 ILT; Group 2 (n= 8) received 5g/kg/d n-6 lipid; Group 3 (n=10) received 10g/kg/d n-6 lipid. Piglets underwent terminal laparotomy to measure bile flow and collect samples. Comparison was made to Group 4 (sow fed), the nutritional gold standard.

**Results:** Comparisons by ANOVA are shown in the Table. Group 3 developed PNALD with increased bilirubin and reduced bile flow. There was no difference in weight gain between TPN groups; however the change, from baseline, in albumin levels were highest for group 3.

**Conclusions:** Both n-6 and n-3 parenteral lipid restriction protect against early onset PNALD, compared to conventional higher dose n-6 lipid therapy. However, in rapidly growing neonates low dose lipid therapies do not provide adequate non-protein energy, indicated by failure to increase plasma albumin over time. Further investigation is required to understand the mechanisms of action of lipid restriction to prevent PNALD and to evaluate the potential long-term risks in growing neonates.
<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (µM/L)</td>
<td>7.0</td>
<td>10.8</td>
<td>56.8</td>
<td>8.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bile Flow (µg/gliver/min)</td>
<td>1.2</td>
<td>0.8</td>
<td>0.1</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>4.9</td>
<td>4.6</td>
<td>4.9</td>
<td>6.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight change (kg)</td>
<td>2.7</td>
<td>2.4</td>
<td>2.7</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>14.0</td>
<td>15.1</td>
<td>20.9</td>
<td>32.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin change (g/L)</td>
<td>-2.2</td>
<td>1.0</td>
<td>9.2</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

288 RACIAL DIFFERENCES BETWEEN OXIDATIVE STRESS AND METABOLIC RISK FACTORS IN LEAN AND OBESE YOUTH. Joshua Warolin\(^1\), Maciej S. Buchowski\(^2\), Sari Acra\(^1\), \(^1\)Pediatric Gastroenterology, Vanderbilt University, Nashville, TN; \(^2\)Medicine, Vanderbilt University, Nashville, TN

Objective: Recent research in children and adolescents has demonstrated significant correlations between markers of oxidative stress and adiposity, obesity-related metabolic abnormalities, adipokines and hypertension. However, it is not fully known if racial differences exist in these demonstrated associations.

Study Design: A marker of oxidative stress (F2-isoprostane) and metabolic risk factors were measured in Caucasian (CaA, \(n=76\)) and African American (AfA, \(n=82\)) youth (8-17 years) recruited over a wide range of BMI percentiles (ensuring similar numbers of normal weight, overweight, and obese participants).

Results: Baseline data in AfA youth displayed significantly lower plasma triglyceride levels than CaA youth (\(p=0.02\)), with significantly higher mean systolic and diastolic blood pressure (\(p=0.02\) and \(p=0.01\), respectively). No racial differences were seen in baseline percentage body fat (\(p=0.85\)) or leptin (\(p=0.28\)); however, both were positively correlated with F2-isoprostane levels.

Utilizing separate linear models and adjusting for gender, age, and Tanner stage, AfA youth varied from CaA youth in the association of oxidation stress with diastolic blood pressure (\(p=0.04\)). However, no racial differences were demonstrated in the association of oxidation stress with percent body fat (\(p=0.88\)), HOMA-IR (\(p=0.18\)), mean systolic blood pressure (\(p=0.63\)), or leptin (\(p=0.29\)).

Conclusions: Consistent with the current literature, oxidative stress levels in our cohort of AfA and CaA youth, as measured by F2-isoprostane, were positively correlated with percent body fat, adipokines, and several obesity-related metabolic abnormalities. However, significant racial differences were only demonstrated in the association of oxidative stress with mean diastolic blood pressure.

289 PROTEIN SYNTHESIS IN SKELETAL MUSCLE OF NEONATES IS ENHANCED BY ADMINISTRATION OF AN AMINO ACID METABOLITE. Scott M. Wheatley\(^1\), Samer El-Kadi\(^1\), Agus Suryawan\(^1\), Claire Boutry\(^1\), Renan A. Orellana\(^1\), Hanh V. Nguyen\(^1\), Steven R. Davis\(^2\), Teresa A. Davis\(^1\)

\(^1\)Children's Nutrition Research Center, Baylor College of Medicine, Houston, TX; \(^2\)Abbott Nutrition, Columbus, OH

Preterm infants are at risk for failure to thrive, secondary to their inability to achieve adequate protein intake as well as medical issues that are characteristic of their immaturity. We have shown that parenteral and enteral administration of the amino acid (AA) leucine stimulates protein synthesis in skeletal muscle of the neonate but less is known of the effects of amino acid metabolites on muscle protein synthesis in the neonate. Overnight fasted neonatal pigs (5-7 days old) were infused with either 0 (AA0), 20 (AA20), 100 (AA100), or 400 (AA400) µmol/kg/hr of the AA metabolite for 1 h. At the end of the infusion, fractional protein synthesis rate and translation initiation activation were determined. Concentrations of the AA metabolite increased with infusion (\(P<0.05\)) and were 10, 98, 316, and 1400 nmol/ml for the AA0, AA20, AA100, and AA400 pigs. Fractional protein synthesis rate in the longissimus dorsi (LD) muscle increased in response to AA infusion, with both AA20 and AA100, but not AA400, higher than AA0 (\(P<0.05\)). Phosphorylation of S6K1 and formation of the active eIF4G-eIF4E complex, regulators of translation initiation, were greater in the AA20 and AA100 than the AA0 group (\(P<0.05\)). These results suggest that supplementation with an AA metabolite enhances protein synthesis in skeletal muscle of the neonate by stimulating translation initiation. (Supported by Abbott Nutrition)

290 INTESTINAL REHABILITATION CENTERS: ARE FEEDING PRACTICES THE SAME? Rebecca J. Wilhelm, Kristen O'Driscoll, Misty Troutt, Samuel Kocoshis, Gastroenterology, Hepatology & Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

BACKGROUND: Feeding disorders generate challenges amongst the Intestinal Failure (IF) population. The reception of alternate formed nutrition can result in children experiencing and/or developing oral aversion. Historically, no formal protocol or guidelines for introduction of solids or avoidance of foods in this population has existed. A survey was generated and distributed to multiple Pediatric Intestinal Failure Consortium (PIFCON) centers to elucidate current feeding strategies.
METHODS: A focused questionnaire was designed by a Registered Dietitian (RD), Speech Pathologist and a Gastroenterologist from our intestinal rehabilitation program. Fifteen PIFCON centers were emailed a survey using Adobe™ distribution. Data were collected related to introduction of solids, avoided foods, percentage of IF population with oral aversion as well as formula types provided to IF patients. RESULTS: Respondents were 8 RDs and 2 Medical Doctors. Amongst the responding centers, two-thirds stated that 50-75% of their IF population under the age of 3 is orally averse. Fifty percent of these centers placed no limitations on solids, whereas the others limited intake of simple sugars. Three quarters followed AAP guidelines for introduction of solids. With regard to formula preferences, practices were quite uniform represented by election to use elemental formula when breast milk is unavailable. CONCLUSION: Based on these preliminary survey results, a consensus protocol is seems to be utilized by participating centers. With a few noted exceptions; consistency in introduction of oral solids was reported. Expansion on this preliminary work is planned to evaluate enteral feeding in regard to advancement and formula usage.

291 TREATMENT OF HOSPITALIZED SEVERELY MALNOURISHED CHILDREN IN DEVELOPED COUNTRIES: MODIFIED THERAPEUTIC FEEDS USING COMMERCIALLY AVAILABLE FORMULAS TO APPROXIMATE STANDARD WORLD HEALTH ORGANIZATION (WHO) THERAPEUTIC FEEDS. Tracy Winder1, Erika M. Davies1, Stacey A. Finch1, Blanca Hernandez1, Mia Neeb1, Anne T. Rabjohn1, George J. Fuchs2,1, 1Department of Clinical Nutrition, Arkansas Children's Hospital, Little Rock, AR; 2Department of Pediatrics, University of Arkansas Medical Sciences College of Medicine, Little Rock, AR

The literature on treatment outcomes of children with severe malnutrition in developed countries indicates a risk of mortality of up to 50%. The World Health Organization's two formula mixes, F-75 and F-100, are considered the "gold standard" in the initial and rehabilitation treatment phases, respectively, of hospitalized children with severe malnutrition in developing countries. Prepared versions of WHO therapeutic feeds are not commercially available in developed countries, therefore commercial infant and pediatric formulas are currently used to treat malnourished children. However, the macro- and micronutrient content of commercial formulas has never been compared to the WHO therapeutic feeds to determine if they provide adequate or optimal nutritional therapy for severe malnutrition in children. A Microsoft® Excel program was developed to enable precise modifications and micronutrient supplementation requirements using different commercially available infant and pediatric formulas necessary to approximate the WHO F-75 and F-100 formula mixes. Hypothetical patients were created in five different age groups. Patients weighing ≤10kg and >10kg were assigned the modified therapeutic infant feed and modified therapeutic pediatric formula feed, respectively. Results of the comparisons revealed that commercially available formulas plus AquAdek™ and additional potassium, magnesium, zinc, copper, selenium, folic acid, and Vitamin D is needed to approximate F-75 and F-100 standards. This Excel program enables practitioners to modify and optimize standard commercial infant and pediatric formulas for treatment of severely malnourished children in developed countries.

292 PARENTAL PERCEPTIONS OF A MOTIVATIONAL INTERVIEWING-BASED PEDIATRIC OBESITY PREVENTION INTERVENTION. Jennifer Woo Baidal1, Sarah Price2, Elizabeth Gonzalez-Suarez3, Matthew W. Gillman2, Kathleen Mitchell4, Sheryl L. Rifas-Shiman2, Christine Horan2, Steven L. Gortmaker5, Elsie M. Taveras2, 1Gastroenterology/Nutrition, Boston Children's Hospital, Boston, MA; 2Obesity Prevention Prog, Harvard Med School/HPHCI, Boston, MA; 3Dana-Farber Cancer Institute, Boston, MA; 4Harvard Vanguard Medical Associates, Boston, MA; 5Harvard School of Public Health, Boston, MA

Background: Motivational interviewing (MI) is an effective communication strategy for behavior change. Few existing studies address parental perceptions of MI for childhood obesity management.

Objective: To examine correlates of parental perceptions of helpfulness and satisfaction with a MI-based intervention.

Methods: We studied the intervention arm of High Five for Kids, a RCT of 2-6-year-olds with BMI ≥ 85th percentile. Using MI principles, nurse practitioners (NPs) delivered the bulk of the intervention at structured study visits. At 1 year parents reported helpfulness of visits in making chosen behavior changes and satisfaction with the intervention.

Results: Of the 253 children, 47% were white, 28% black, and 19% Hispanic; 58% of parents had a college degree, and 65% had household incomes ≥ $50,000/year. At 1 year, parents reported NP visits as "a lot" helpful (v. some/not very much) in decreasing child's TV viewing (49%), sugary beverage intake (66%), and fast food intake (63%). In multivariable models, parents with BMI ≥ 30 (v. <30) kg/m2 perceived MI-based visits as "a lot" helpful in reducing child sugary beverage intake (OR 2.86). Household income of $50K or less (v.>$50K) correlated with parent perception of MI-based visits as "a lot" helpful in reducing child TV viewing (OR 3.60). Foreign-born (v. US-born) parents perceived MI-based visits as "a lot" helpful in reducing child TV viewing (OR 8.81) and sugary beverage intake (OR 3.32). The intervention increased satisfaction with primary care for 62% of parents. Parents of female (v.
Abstracts

male), black (v. white), and Latino (v. white) children had lower reports of intervention satisfaction.

**Conclusions:** Our findings support the need to consider socio-demographic factors in the design of childhood obesity interventions.


**Background:** Racial/ethnic minority children are disproportionately burdened by obesity. Minorities who immigrate to the US as adults have low obesity prevalence on arrival, but how race/ethnicity interacts with immigration status in children is unknown.

**Objective:** To examine racial/ethnic differences in obesity and BMI trajectory characteristics among children of US-born and immigrant mothers.

**Methods:** We prospectively studied 697 white, 184 black, 45 Hispanic, and 38 Asian mother-child pairs in Project Viva. Main outcomes were BMI z-score and obesity (BMI ≥ 95th %ile) at age 7 years, and characteristics of BMI trajectories from birth to age 7. We used multivariable linear and logistic regression models to assess differences in outcomes within maternal US-born and maternal immigrant groups, adjusting for age, sex, and family socioeconomic status.

**Results:** 792 mothers were US-born and 172 were immigrants. At age 7, obesity prevalence was 7% in whites, 27% in blacks, 24% in Hispanics, and 0% in Asians. In multivariable models, among children of US-born and immigrant mothers, black children had higher mean 7-y BMI z-score (0.37 and 0.30 units, respectively) and higher odds of obesity (OR 2.84 and 3.31) than whites. In children of both US-born and immigrant mothers, Asian children had younger mean age at the infancy BMI peak (-0.95 and -0.62 mo, respectively), lower mean BMI at adiposity rebound (-0.99 and -0.6 kg/m2), and steeper decrease in BMI velocity from infancy peak to adiposity rebound (-0.79 and -0.38 kg/m2/mo) when compared to white counterparts.

**Conclusions:** Higher obesity prevalence and higher BMI were evident among black children of both US-born and of immigrant mothers when compared to their white counterparts. Asian children had infancy and early childhood BMI trajectories that led to lower risk of obesity than whites in mid-childhood.

**294 FACTORS PREDICTING VITAMIN D DEFICIENCY IN CHILDREN WITH INTESTINAL FAILURE.** Govardhana Yannam2, Katie Williamson1, Vasu Manimaran3, Linda Wilkinson1,2, Donna Bartle2, Carroll Harmon2, Reed A. Dimmitt1,2, 1Pediatrics, University of Alabama at Birmingham, Birmingham, AL; 2Surgery, University of Alabama at Birmingham, Birmingham, AL

**BACKGROUND:** Patients with intestinal failure (IF) may have inadequate absorption of Vitamin D. The goal of this study was to determine patient factors associated with Vitamin D deficiency.

**METHODS:** We reviewed the clinical data from patients recently weaned from parenteral nutrition (PN) in the Georgeson Center for Advance Intestinal Rehabilitation (GCAIR). Patient demographics, length of remaining small and large bowel, presence of intact ileocecal valve and time on PN were collected in all patients from a prospective GCAIR database. Serum levels of 25-OH vitamin D were measured for each patient one month after PN weaning. The Wilcoxon rank sum test for medians and Fischer's exact for proportions were used for the statistical analysis of factors predicting vitamin D deficiency. A p<0.05 was considered significant.

**RESULTS:** A total of 68 children receiving vitamin D supplements met the criteria. Mean age was 4.4 years. Thirty three (48%) were females, 25 (36%) were Caucasian, and 35 (51%) were African American. Median days on PN, median length of small bowel remaining, median percentage of colon remaining and percent of intact ileocecal valve were 287 days, 82.5 cm, 100.0% and 57.8% respectively. Thirty (44%) patients were found to have Vitamin D deficiency. Older patients receiving TPN for more days was predictive of Vitamin D deficiency (Table).

**CONCLUSIONS:** There was a high prevalence of Vitamin D deficiency in children with IF. Patient demographic data or residual length of bowel was not predictive of deficiency. Our findings would support universal Vitamin D analysis in patients following weaning of PN.

<table>
<thead>
<tr>
<th>Comparison of demographic and clinical characteristics of children by Vitamin D deficiency</th>
<th>Vitamin D Sufficient</th>
<th>Vitamin D Deficient</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>4.1</td>
<td>5.7</td>
<td>0.019</td>
</tr>
<tr>
<td>Median days on TPN</td>
<td>208</td>
<td>365</td>
<td>0.05</td>
</tr>
</tbody>
</table>
295* THE IMPACT OF SUPPLEMENTAL NASOGASTRIC TUBE NUTRITION ON HEIGHT AND WEIGHT IN PEDIATRIC CROHN'S DISEASE. Dale Lee1, Kelly E. Kachelries1, Kernika Gupta1, Monica Lorusso2,1, Krista M. Whitehead1, Rita M. Herskovitz1, Mary B. Leonard1, Robert N. Baldassano1,1, Children's Hospital of Philadelphia, Philadelphia, PA; 2Meyer Children's Hospital, Florence, Italy

Background: Growth delay and poor nutritional status are commonly present in children with Crohn's disease (CD).

Methods: A prevalent cohort of 138 pediatric CD patients was prospectively followed to evaluate bone density and body composition. Data was collected at a baseline visit, 6, and 12 months. Families specified the number of days of NG feeding supplementation per week, and 24 hour dietary recalls were performed after each study visit. Our analysis included patients age 10-18 years old (n=116). We defined 2 groups of subjects: those receiving a high level of NG supplementation (which we defined as NG feeds at least 4 days a week for at least 6 months, n=16), and those receiving either lower/no supplementation (n=100). Paired and un-paired t-tests were used to compare differences within and between groups. We report z-scores with means +/- SD.

Results: At the initial visit, patients on high NG supplemental feeds had significantly lower mean height z scores (-1.66 +/-0.86 vs. -0.71 +/- 0.99; p= 0.0004) and mean weight z scores (-1.41 +/-1.41 vs. -0.47 +/-1.09; p=0.003). Over 12 months, the high NG supplementation group had a greater increase in height z score (0.86 +/-0.44 vs. 0.61 +/- 0.40; p=0.03), and a greater increase in weight z score (0.89 +/-0.72 vs. 0.57 +/-0.58; p=0.06). Yet at 12 months, the groups continued to show significant differences in height and weight z scores. Mean albumin was similar at baseline for both groups (high NG 4.0 vs low/no NG 4.3; p=0.10), and neither group had a significant change in mean albumin over 12 months (high NG 0.2, p=0.10; and low/no NG -0.03, p=0.57)

Conclusion: NG supplemental feeds are associated with more rapid improvements in height and weight z-scores in children with CD. Supplemental nutrition may play a key role in the management of growth in pediatric CD.

296 TO ESTABLISH A CORRELATION BETWEEN BRACHIAL PERIMETER AND OTHER ANTHROPOMETRICAL MARKERS IN A NUTRITIONAL ASSESSMENT APPLIED TO 0-5 YEARS OLD CHILDREN, MEXICO CITY. Flora Zárate1, Carmen Torres1, Mariana Tirado1, Luisa Diaz2, Alejandro Valderrama1, Roberto Cervantes1, Ericka Montijo1, Jose Cadena1, Monserrat Cazares1, Erick Toro1, Jaime Ramirez1, Gastroenterology and Nutrition, Instituto Nacional de Pediatría, Mexico City, Mexico; 1Methodology, Instituto Nacional de Pediatría, Mexico, City, Mexico; 2Endocrinology, Instituto Nacional de Pediatría, Mexico, City, Mexico

Objective To determine the correlation between brachial perimeter and other anthropometric indicators in nutritional assessments applied to 0-5 year old children with edema, ascites, and/or visceromegaly. Methods: A descriptive, observational, and transversal study carried out with samples collected from 100 children, who were hospitalized at the National Institute of Pediatrics (INP), in Mexico City. Measurement of weight, height, cephalic perimeter, brachial or paramesobrachial perimeter (BP or PMBP), tricepal fold were made. The assessment of weight/height (W/H), weight/age (W/A), height/age (H/A), cephalic perimeter (CP), and paramesobrachial perimeter (PPMB) were made using Z-score, Quaker Arm Circumference measuring stick (QUAC) method for brachial perimeter, and Kanawati McLaren index. Results: The principal clinical characteristics found were: Hepatomegaly in 79%, splenomegaly in 39%. In accordance with Z-score (WHO), W/A measurement showed that 86% of the patients were found with malnutrition, for H/A it was 74%, and for W/H it was 64% while for PMBP it was 90%. With the QUAC method 87% was found with malnutrition while Kanawati McLaren index showed 81%. All the anthropometric indicators detected severe malnutrition between 31 to 51%. Discussion: The indicator H/A depicted a considerable prevalence of malnutrition and all the indicators detected severe malnutrition in a high percentage of the patients. Suggesting that the patients studied were crossing with chronic pathologies. PMBP, QUAC method and Kanawati McLaren index compared with the habitual indicator (W/H) showed to be a better indicator for malnutrition. Conclusions: The applicability of the most used habitual indicator for the assessment of acute malnutrition grade (W/H) in clinical situations in children with ascites, edema, and/or visceromegaly decreased due to the fact that it is affected by weight; underestimating the malnutrition grade of such patients. Based on this, we suggest the use of PMBP and QUAC method as well as Kanawati McLaren index in this group of patients.

Motility/Functional Gastrointestinal Disorders

303 DIAGNOSTIC UTILITY OF "RED FLAGS" IN DETECTING ORGANIC GASTROINTESTINAL DISEASE IN CHILDREN: A PROSPECTIVE STUDY. Jeremy P. Middleton1, Cary G. Sauer1, Manu R. Sood2, Pediatric Gastroenterology, Hepatology and Nutrition, Emory University, Atlanta, GA; 2Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI

Objectives: Clinicians evaluating children with gastrointestinal symptoms often use the presence of alarm symptoms, or red flags, to prompt further evaluation. Rome III criteria suggest that patients with functional gastrointestinal disorders (FGIDs) lack these alarm symptoms. The objective of this study was to prospectively
evaluate the diagnostic utility of red flags while secondarily determining the frequency of red flag symptoms in children with FGIDs.

Methods: An IRB-approved prospective questionnaire study was performed in children presenting for initial diagnostic endoscopy, as determined by their primary gastroenterologist. The parents were asked to fill out a modified Rome III Diagnostic Questionnaire for Pediatric FGIDs that included inquiry of eleven red flags. Patients fulfilled criteria for organic disorder for all abnormal histopathology.

Results: The patient population was 56% female with a mean age of 13 (8-18), and 26 patients met Rome III criteria for FGID. There was abnormal histopathology in 24 of 50 cases (48%) with eosinophilic gastrointestinal disease (27%), active gastritis (18%) and acute duodenitis (14%) being most common. Forty-four of 50 (88%) patients reported at least one red flag. The most frequently reported red flag was nocturnal pain (70%), hematochezia (62%) and nocturnal stooling (58%). For patients with at least one red flag, the sensitivity of predicting an organic gastrointestinal disorder was 91%. Those red flags with the highest positive predictive value were arthritis (100%), nocturnal stooling (88%) and hematochezia (78%). Of the 26 patients with FGIDs, 23 (88%) reported red flags.

Conclusion: Red flags are useful tools to prompt further evaluation with endoscopy. Those red flags most predictive of organic disease are arthritis, nocturnal stooling and hematochezia. The presence of red flags does not rule out FGIDs.

304 EVALUATION OF PRESSURE PAIN THRESHOLD IN CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN. Ismaeel Hashemi¹, Steven Harte¹, Dan Clauw¹, Afton Hassett¹, Emilia Mondragon¹, Miranda van Tilburg², Majdi Abu-Salih¹, ¹University of Michigan, Ann Arbor, MI; ²University of North Carolina, Chapel Hill, NC

Background: Chronic functional abdominal pain (FAP) affects 15% of children. Children with FAP demonstrate decreased threshold of evoked visceral pain, but assessment of visceral pain sensitivity is difficult and invasive. The aim of this pilot study was to noninvasively evaluate somatic pressure pain threshold (PPT) at an asymptomatic site distal from the abdomen in children with FAP, to determine if this measure is also abnormal in FAP and is reflective of a generalized disturbance in pain processing ("central sensitization").

Methods: Patients were recruited from the UM Pediatric GI Clinic after receiving a diagnosis of FAP using the Rome III diagnostic criteria. Age and gender-matched children were recruited as healthy controls. PPT was determined by applying an ascending series of pressures (5-s duration, 25-s intervals) beginning at 0.10 kg/cm² and increasing in 0.10 kg/cm² intervals to the dominant thumbnail. Participants were asked "Did that hurt?" Negative responses elicited delivery of the next higher pressure intensity. The first positive response or a maximum pressure of 5 kg/cm² ended the test. This series was repeated after a 1 min interval. The mean pressure intensity (kg/cm²) reported as painful from both series was calculated.

Results: 8 patients (6 female, age 10.5±1.4 (SD) yr; 2 male, mean age 11.5±0.7 yr) and 24 controls (10 female, age 10.2±1.5 yr; 14 males, age 9.6±1.4 yr) were recruited. Children with FAP had reduced PPT (mean 1.1kg/cm²) compared to healthy controls (mean 2.1kg/cm²; p=0.002). There was no difference in PPT between male (2.0 kg/cm²) and female (2.1 kg/cm²) healthy controls.

Conclusion: Even in this small sample, somatic PPT was markedly reduced in children with FAP compared to healthy controls. This suggests that FAP may be a diffuse disturbance in central nervous system pain processing. There was also no difference in PPT between healthy pre-pubertal males and females, which is in contrast to healthy adults where females typically exhibit significantly lower PPT than males.

305 INFLUENCE OF SPINAL FUNCTION AND INTEGRITY ON ANORECTAL RESPONSES IN CHILDREN WITH SPINAL CORD MALFORMATIONS. Lusine Ambartsumyan¹, Stuart Bauer², Karen Murray³, Samuel Nurko¹, ¹Gastroenterology, Boston Children's Hospital, Boston, MA; ²Urology, Boston Children's Hospital, Boston, MA; ³Gastroenterology, Seattle Children's Hospital, Seattle, WA

Background: Anorectal function (AF) may be abnormal in patients with spinal cord malformations (SCM) but how AF varies according to different neurologic lesions is not clear. The aims were to compare anorectal responses in patients with SCM with those of healthy controls and to correlate changes in AF with the functional level of the lesion by neurological examination (NE) and urodynamic studies (UDS). Methods: Anorectal manometries of children with SCM, who had previously undergone UDS, were reviewed. UDS was used to divide patients into upper motor (UMN), lower motor (LMN), and mixed motor (MMN) neuron lesions. NE was used to divide patients into thoraco-lumbar (TL) and sacral (SL) lesions. Tracings were correlated with the functional level of the spinal lesions and the UDS findings, and compared with controls. Results: 41 children (mean age, 142 ± 110.9 months) with SCM and 18 controls (mean age, 117 ± 72.8) were included. NE identified 23 TL and 18 SL lesions. UDS identified 12 UMN, 25 LMN, and 4 MMN lesions. The rectoan inhibitory reflex (RAIR) was present in all patients. SCM group had increased amplitude and longer duration of internal anal sphincter (IAS) relaxation. The % of maximum IAS relaxation was higher in the SCM group. SCM group had abnormalities in sensation and squeeze. SL group had increased amplitude and longer duration of IAS relaxation. IAS resting pressure, sensation, and squeeze did not differ between TL and SL groups. There were no significant differences between UMN, LMN, and
MMN groups. Conclusions: Children with SCM had abnormalities in anorectal manometry. Differences in RAIR characteristics between SCM and controls suggest that RAIR is modulated by spinal influences. NE may be superior to the UDS in identifying type of bowel dysfunction in SCM. We speculate that these abnormalities in RAIR function may be responsible, in part, for the different defecation abnormalities in children with neurogenic bowel dysfunction.

306 CHRONIC ABDOMINAL PAIN: PERCEPTIONS AND PRACTICES IN PRIMARY CARE PEDIATRICS. Jennifer V. Schurman\(^1\), Emily D. Kessler\(^2,3\), Craig A. Friesen\(^3\), \(^1\)Section of Developmental & Behavioral Sciences, Children's Mercy Hospitals & Clinics, Kansas City, MO; \(^2\)Clinical Child Psychology Program, University of Kansas, Lawrence, KS; \(^3\)Section of Gastroenterology, Children's Mercy Hospitals & Clinics, Kansas City, MO

Background. Chronic abdominal pain (CAP) is a common complaint among children and adolescents. Most children with CAP (>90%) do not evidence clear organic disease, and no clinical practice guidelines (CPGs) exist for treating this population of children with functional pain and symptoms. This study examined the practices used by primary care pediatricians (PCPs) to assess and treat CAP, as an initial step in guiding CPG development. Methods. A survey was mailed to a random sample of office-based pediatrician members (PCPs) of the American Medical Association. PCPs (n=470) provided information about the typical presentation of CAP and assessment/treatment approaches used in their own practice. PCPs also were asked to provide a definition of a functional gastrointestinal disorder (FGID) and rate their familiarity with the Rome Criteria for diagnosing FGIDs. Results. The majority of PCPs (54%) reported 10% or more of their patients complain of CAP. Commonly perceived causes were constipation (53%), functional pain (29%), and stress/anxiety (17%). Frequently used assessment strategies included blood tests (75%) and urine tests (72%). Most PCPs (80%) endorsed using both behavioral/coping and medical/physiological treatments, but the specific treatments varied. Most (73%) FGID definitions included lack of organic etiology as a defining feature, but otherwise were highly variable. The Rome Criteria was familiar to less than half (42%) of PCPs and only 7% reported using these for diagnosis in clinical practice. Conclusions. Perceptions and practices of pediatric CAP varied widely among PCPs; no single standard of care emerged to guide development of a CPG for this population. Future research should evaluate the efficacy of specific strategies currently in use to identify potential opportunities for improving assessment and treatment of pediatric CAP in primary care.

307 RETCHING: A PREDICTOR OF DELAYED GASTRIC EMPTYING IN CHILDREN. Hilary Jericho, Papa Adams, Gang Zhang, Miguel Saps, Department of Pediatric Gastroenterology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

Background: The gastroparesis cardinal symptoms index (GCSI) is a reliable and valid tool to predict delayed gastric emptying (DGE) in adults. There are no validated diagnostic tools to diagnose gastroparesis in children. Validation of the GCSI in children would provide a cost effective, rapid, and reliable method for evaluating DGE and monitor progress. Objectives: Primary: Validation of the GCSI in children. Secondary: 1- Assess understanding of the symptoms in the GCSI, and: 2- Investigate the predictive value of all symptoms of the GCSI for DGE.

Methods: Symptomatic children referred for nuclear gastric scintigraphy (NG) completed: 1- Ten question GCSIs (Likert scale with numbers and words separately to assess differential predictive value); 2- Established comprehension of each of the 10 questions at the time of the NG (0 lack of, 1 little, 2 mostly-3 complete understanding). NG was performed following ANMS-NM protocol and diagnostic criteria.

Results: 42 children (30 F), 5-18 years (29 children >12 years). 67% had normal NG. Strong correlation found between symptom severity results obtained word and numerically based (r: 0.825-0.946, p=0.01). Neither GCSI scores, nor any symptoms in the GCSI predicted DGE with exception of retching (P=0.002). Children reported understanding of most terms of GCSI (average score 2.4). Pain was the term with highest understanding while retching was the least understood term (mean 1.7, 43% scored l-2). Lack of understanding of retching: 38% in children <12 years vs.24% >12 years. Children reported understanding of all other terms. Excluding symptoms that were not understood for each child did not significantly improve symptoms' predictive values.

Conclusion: The GCSI does not predict DGE in children. Lack of predictive value does not seem to be related to lack of understanding. Only the individual symptom of retching predicted DGE but this term was frequently reported as poorly understood. Additional studies using a larger patient population are necessary to validate this data.

308 THE ROLE OF PELVIC FLOOR MUSCLE EXERCISES IN MAINTENANCE THERAPY OF CONSTIPATION IN CHILDREN. Vajiheh Modaresiaryazdi\(^1\), Bahar Pakseresht\(^2\), Zalfa Modarres\(^3\), \(^1\)Shohada Hospital, Social Security Organization, Yazd, Islamic Republic of Iran; \(^2\)Faculty of Pharmacy, Shahid Sadough University of Medical Sciences, Yazd, Islamic Republic of Iran; \(^3\)Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

PURPOSE: Animated biofeedback effectively treats bowel and voiding dysfunction in children with dysfunctional contractions of the pelvic floor muscles. Maintenance therapy is crucial for long-term success. This study aimed to evaluate the role of pelvic floor muscle exercises (PFME) in children with constipation.

Methods: A retrospective chart review of children (n=30) with constipation treated with PFME as maintenance therapy. Characteristics of PFME included frequency, duration, and repetition of exercises. Outcome measures included clinical improvement in symptoms and need for medications.

Results: The majority of children (80%) showed improvement in symptoms and reduction in number of medications. Compliance with PFME was high, with an average of 3-4 sessions per week.

Conclusion: PFME are an effective and safe maintenance therapy for children with constipation. Further research is needed to determine optimal treatment parameters.
voiding and or intractable constipation. We evaluated the efficacy of simple method of pelvic floor muscle exercises
including squeezing plastic bottle of water during bowel movement by suffering children in maintenance therapy of
constipation in children with functional constipation.
MATERIALS AND METHODS: A total of 80 children aged 2-5 years, with functional constipation according to
Rome III criteria were assigned into two groups of 40 subjects, randomly. After initial disimpaction, both groups
received 1gr/kg polyethylen glycol powder and 60-300 mg senna syrup; based on their age and weight once daily.
All parents also trained to change their children's life style including behavioral and diet modification (hydration,
high fiber diet, daily toilet). In addition group 2 trained for doing pelvic floor muscle exercise by squeezing plastic
bottle of water during bowel movement and also 3 times per day. Successful treatment was defined as restore normal
bowel habit and using toilet without fear. Subjects were evaluated for response to the treatment after 1, 3, 6 months.
RESULTS: Group 2 showed higher success rate compared to conventional therapy alone which was done in group
1(90% vs 80%), in addition normal bowel habit started sooner in group 2. 87.5% of subjects in group 2 and 75% of
subjects in group 1 were symptom free after 6 months.
CONCLUSIONS: Simple method of pelvic floor muscle exercises including squeezing plastic bottle of water during bowel
movement and as daily activity in children suffering from functional constipation is beneficial to improve
bowel habit movement and maintenance therapy of functional constipation.

309 CALRETININ HISTOCHEMICAL STAINING ON ENDOSCOPIC MUCOSAL BIOPSIES IS A
HIGHLY SPECIFIC DIAGNOSTIC MARKER FOR HIRSCHSPRUNG'S DISEASE (HD).
Silvana Bonilla, Alejandro Flores, Barbara Weinstein, Tufts University, Boston, MA; Pathology, Tufts University, Boston, MA
Background: The diagnosis of HD is sometimes difficult to establish. Full-thickness biopsy (FTB) of the rectum
including rectal mucosa and underlying muscle, remains the gold standard in the diagnosis of HD. FTB is not
exempt of complications including perforation, bleeding and infection. Other tests described in the diagnostic
workup of HD include contrast enema (CE), anorectal manometry (ARM) and rectal suction biopsy with
acetylcholinesterase histochemical staining (AHS). Multiple antibodies have been reported to highlight ganglion
cells and improve nerve fiber identification in biopsies. Calretinin histochemical staining (CHS) has been shown to
be superior to AHS as an adjunct in the diagnosis of HD.

Aim: To explore the value of CHS as a diagnostic tool for HD compared to endoscopic mucosal biopsies (EMB)
stained for hematoxylin-eosin (H-E), ARM and CE in patients suspected of having HD.
Study design: We reviewed records of 28 pediatric patients suspected of having HD who underwent EMB (H-E and
CHS) and at least one of the following tests: CE and/or ARM. The sensitivity and specificity of CHS, EMB stained
for H-E, ARM and CE to detect HD was calculated.
Results: 28 patients suspected of having HD were included in the study. All 28 patients had positive CHS of
intrinsic nerve fibers (specificity of 100%). Similarly, among the 26 patients who underwent ARM, all showed a
normal rectoanal inhibitory reflex, also corresponding to 100% specificity. 17 patients (61% specificity) did have
identifiable ganglion cells in biopsy. The remaining biopsies were superficial without submucosa, giving inadequate
tissue to diagnose HD based on absence of ganglion cells. Among the 21 patients who underwent CE, 16 showed
normal anatomy (76% specificity) whereas 5 showed findings concerning for HD.
Conclusion: In a population of patients suspected of having HD, CHS on EMB is a highly specific diagnostic
marker for HD. Future investigations should estimate the sensitivity of this tool by including patients with confirmed
HD.

310 A NOVEL TECHNIQUE FOR ONE STEP LOW PROFILE CECOSTOMY PLACEMENT.
Sarah E. Catalano, Peter D. Ngo, Carl-Christian Jackson, Walter Chwals, Alejandro Flores, Tufts University School of
Medicine, Boston, MA; Division of Pediatric Gastroenterology, Floating Hospital for Children at Tufts Medical Center,
Boston, MA; Division of Pediatric Surgery, Floating Hospital for Children at Tufts Medical Center, Boston, MA
Background and Aims: Cecostomy placement to provide antegrade colonic enemas (ACE) is a treatment option for
children with defecation disorders refractory to medical management. This is the first description of a combined
laparoscopic and endoscopic technique to place a low profile cecostomy. Colonoscopy allows for a more precise
placement of transcecal sutures and less traumatic tract dilation and cecopexy allows for primary low profile device
use, thereby preventing the need for repeat anesthesia with cecostomy tube conversion.
Methods: Retrospective review of laparoscopic assisted percutaneous endoscopic cecostomy with primary button
placement (LAPEC-PBP) at a single institution from 2010-2012.
Results: 24 patients were included (50% female, mean age 9.4 years, mean follow-up 8.7 months). All patients had
chronic constipation with soiling, 1 patient had Hirschsprung's disease. Colonic manometry was performed in 97%
and was abnormal in 87%. The single intraoperative complication was a cecal serosal tear repaired with a
laparoscopic suture. Mean length of hospital stay was 4.3 days. Cecopexy sutures were removed on postoperative
day 12± 2.5. The mean number of GI motility/laxative medications used preoperatively was 2.0 and postoperatively
was 2.7 with a mean of 2 given via cecostomy. The most frequent preoperative medications were PEG (75%),
lubipristone (50%) and the most common medications used for ACE were normal saline (79%) and glycerin (63%). Postoperative complications included 1 patient with cecostomy tube cellulitis requiring IV antibiotics, 1 patient with a suture site abscess requiring surgical drainage and IV antibiotics, and 1 dislodged tube. Conclusions: LAPEC-PBP is a novel and safe procedure eliminating the need for repeat anesthesia with primary tube conversion.

311 EOSINOPHILIC ESOPHAGITIS IN CHILDREN WITH OESOPHAGEAL ATRESIA. Usha Krishnan1, Jasbir Dhaliwal1, Vincent Varjavandi3, Ashish Jiwane2, Ella Sugo2, Avi Lemberg1, Andrew Day1, Vivienne Tobias2,
1Paediatric Gastroenterology, Sydney Children's Hospital, Sydney, NSW, Australia; 2Anatomical Pathology, SEALS at Sydney Children's Hospital, Sydney, NSW, Australia; 3Paediatric Surgery, Sydney Children's Hospital, Sydney, NSW, Australia
Introduction: Eosinophilic Esophagitis (EE) has only rarely been reported in patients with oesophageal atresia (OA). We present a case series of EE in OA patients.
Methods: A retrospective chart review of 110 OA patients between January 1999 and April 2012 at Sydney Children's Hospital.
Results:
14.5%(16/110) of our OA patients had EE (>15 eosinophils/HPF). The average number of eosinophils at diagnosis was 26/HPF (19/HPF-80/HPF). The median age for diagnosis of EE was 1 year 5.5 months (8 months-8 year 7 months). In the EE group 31% had asthma, 12.5% had eczema, 25% had food allergy and 0.06% had peripheral eosinophilia.
10 patients were treated (5 with Budesonide slurry and 5 with swallowed Fluticazon). 7/10 had repeat endoscopies. 3/7 had normal histology and 4/7 had histological improvement. 5/6 patients identified on retrospective review, were not treated for EE but had normal histology on repeat endoscopy on acid suppression alone.
37.5% (6/16) patients had oesophageal stricture at time of EE diagnosis. 3/6 were dilated and 3/6 had resolution of their strictures on medical treatment of their EE alone.
Conclusion: EE was seen in 14.5% of children with OA in this retrospective review. OA patients with EE have a significantly increased risk of developing complications, compared to those without EE. EE should be considered in OA patients with increasing dysphagia and recurrent strictures.

Table 1: Incidence of complications in EE and non EE with OA

<table>
<thead>
<tr>
<th></th>
<th>OA patients with histological evidence of EE (&gt;15/HPF)</th>
<th>OA patients with no histological evidence of EE (difference between EE and non-EE patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphagia</td>
<td>50% (8/16)</td>
<td>7.4% (7/94) [0.0001]</td>
</tr>
<tr>
<td>Reactive Airway Disease</td>
<td>56.3% (9/16)</td>
<td>6.4% (6/94) [0.001]</td>
</tr>
<tr>
<td>Dying Spells</td>
<td>25% (4/16)</td>
<td>3.2% (3/94) [0.008]</td>
</tr>
<tr>
<td>Tracheomalacia</td>
<td>56.3% (9/16)</td>
<td>15.6% (15/94) [0.0003]</td>
</tr>
<tr>
<td>Fundoplication</td>
<td>31.3% (5/16)</td>
<td>10.6% (10/94) [0.042]</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>37.5% (6/16)</td>
<td>10.6% (10/94) [0.0123]</td>
</tr>
<tr>
<td>Aortopexy</td>
<td>25% (4/16)</td>
<td>5.3% (5/94) [0.0246]</td>
</tr>
</tbody>
</table>

312 HIGH PREVALENCE OF NAUSEA IN CHILDREN WITH PAIN-ASSOCIATED FUNCTIONAL BOWEL DISORDERS: ARE ROME CRITERIA HELPFUL? Katja Kovacic, B. U. Li, Sara Williams, Manu Sood, Adrian Miranda, Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI
Background: The presence of nausea in children with chronic abdominal pain may adversely affect social and school functioning. A lack of descriptive studies makes it difficult to recognize clinical patterns.
Objectives: To determine the prevalence of nausea, disability and clinical symptom pattern in pediatric patients with pain-associated functional gastrointestinal disorders (FGIDs) and examine the overlap of FGIDs based on Rome III criteria.
Methods: 221 patients, 69% female, 6-18 years of age, presenting to an outpatient pediatric gastroenterology clinic, prospectively completed a symptom questionnaire. A total of 183 patients with pain-associated FGIDs of 2 months or greater duration were studied.
Results: Our cohort of pain-associated FGID patients had an average pain rating of 6.63. Overall, 105 (57%) complained of nausea. Among these, 53% had nausea 2 times per week and 28% experienced daily nausea.
Frequency of nausea was significantly correlated with poor social (r=0.28, p=.022) but not school (r=0.15, p>0.05) functioning. Over a period of two months, an average of 5 full days of school and 10 days of after-school activities were missed due to nausea. Headache (73%), fatigue (63%), early satiety (69%) and postprandial fullness (49%) were common but only 31% had heartburn. Many of these patients met Rome III criteria for other FGIDs (Table 1). While 84% met adult Rome criteria for functional dyspepsia, only 14% meet the pediatric Rome criteria. There was a remarkable overlap between groups.

Conclusion: Nausea is prevalent in patients with pain-associated FGIDs and correlates with poor social functioning. In this cohort, nausea is a central co-morbid symptom that requires further study. Unfortunately, there is substantial overlap between FGIDs, questioning the validity of the Rome III classification scheme to study these patients.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Functional Dyspepsia</th>
<th>IBS-diarrhea</th>
<th>IBS-constipation</th>
<th>Abdominal Migraine</th>
<th>Cyclic vomiting syndrome</th>
<th>Functional abdominal pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=105</td>
<td>15(14%)</td>
<td>60(57%)</td>
<td>50(47%)</td>
<td>8(8%)</td>
<td>2(2%)</td>
<td>4(4%)</td>
</tr>
</tbody>
</table>

313 NUTRITIONAL PROFILE AND FIBER INTAKE IN CHILDREN WITH FUNCTIONAL GASTROINTESTINAL DISORDERS RELATED TO CONSTIPATION. Christian G. Boggio Marzet, María Luisa Deforel, Susana Dozo, Verónica Schuster, Pediatric Gastroenterology & Nutrition Section, Hospital "Dr.I.Pirovano", Capital Federal, Argentina

Introduction: Few studies in pediatric population concerning fiber intake due to nutritional status in patients with functional gastrointestinal disorders related to constipation (FGDRC) exist.

Objective: To describe nutritional profile of children with FGDRC and associate with fiber intake.

Material and Methods: Sample; 49 children aged 5 to 17 years diagnosed with FGDRC according to Rome III Criteria, establishing subgroups: Functional Constipation (FC) and Irritable Bowel Syndrome with Constipation (IBS-C). Study period: 01-01-11 to 31-12-11. Z scores were estimated for weight, height and body mass index (BMI) according to WHO references adapted by the Argentine Ministry of Health. Nutritional status (NS) was established according to Z score percentile for BMI: Normal (No), (Pc 10 to 85), Underweight (Un) (Pc < 10) and Overweight/Obesity (Ov/Ob) (Pc > 85). Fiber intake was estimated by the formula: age + 5 and adequacy was established according to initial consumption by 24 hour dietary recall.

Results: 44.9% female, 55.1% male, mean age 9 years 5 months ± 3 years 1 month. Diagnosis: a)FC 75.5%, IBS-C 24.4%, no significant differences by gender (Fisher p=0.507) or between children aged 10 and under (Fisher p=1.00), b) NS: Normal 73.4%, (95% CI 61-85), Ov/Ob 21.6% among children with IBS-C and 41.6% among those with FC without enough evidence to differ significantly (Proportion p Test=0.17), with mean height Z score -0.37 ± 1.1, and mean BMI Z score 0.66 ± 1.58. Total fiber intake was inadequate for 98% of the sample with a mean of 6.7 ± 1.58 (95%CI 6.1-7.3) without differences between the two groups (Welch Test p=0.60).

Conclusions: The sample of children with FGDRC showed an overall 26.5% Ov/Ob (95% CI 14-39) with an inadequacy of fiber intake for almost all of the population study (98%) regardless of FGD diagnosis.

314 THE EPIDEMIOLOGY OF ACHALASIA OF THE LOWER ESOPHAGEAL SPHINCTER IN CHILDREN IN SAN DIEGO COUNTY, CALIFORNIA. Rebecca N. Cherry, Neelesh A. Tipnis, Pediatric Gastroenterology, University of California–San Diego, San Diego, CA

Aim: To determine the incidence and examine the epidemiology of achalasia of the lower esophageal sphincter in children in San Diego County, California.

Methods: The 4 regional pediatric surgical centers in San Diego County were asked to provide demographic and epidemiological data on cases of childhood achalasia from 2000 to 2009. Incidence rates were calculated from San Diego County childhood population estimate from the 2010 US Census.

Results: Between 2000 and 2009, 18 children (61% male, mean age at diagnosis was 9.5 ± 5 years) were diagnosed with achalasia of the lower esophageal sphincter. The population of children was estimated to be 726,048 children in 2010. The incidence of achalasia during this time period was 0.24/100,000/children/year (95% CI 0.11—0.28). Of the 18 children, 9 (50%) were Latino-Caucasian; 6 (33%) were non-Latino Caucasian; 2 (11%) were non-Latino Asian; and 1 (6%) was non-Latino African American. Pneumatic dilatation was the primary treatment rendered to 15 (83%) children and cardiomyotomy was the primary treatment in 3 (17%). All but one child managed by pneumatic dilatation required repeat procedures to control symptoms (median 3, range 1-7). One child initially treated by cardiomyotomy also required a single pneumatic dilatation to control symptoms.

Conclusions: This is the first study to evaluate the epidemiology of achalasia in children in the US population. The mean incidence of achalasia in San Diego County from 2000 to 2009 is at least 0.24/10,000 children/year. This number is similar to the incidence of achalasia published for the UK over a similar time period.
315 FOLLOW-UP OF SEVERE CONSTIPATION IN CHILDREN AFTER NORMAL RECTAL BIOPSY FOR HIRSCHSPRUNG'S DISEASE. Khao Tran, Jaime Belkind-Gerson, Brian Surjanhata, Allan Goldstein, Braden Kuo, MGH, Boston, MA

Background and Aim: Severe constipation is a challenge in children. We define pts with severe constipation as those with persistent symptoms who warrant evaluation for Hirschsprung's Disease (HD). Our aim is to examine the long-term outcomes of this population.

Methods: Retrospective chart analysis of children with severe constipation after normal rectal biopsy for HD from 2001-2011. Successful outcome: a period of at least 4 wks with >3 bowel movements per wk, without pain during defecation, or encopresis. Data from GI clinic visits collected at baseline, 3 mo, 1 yr, and 2 yr after biopsy. Pts were placed in appropriate categories: successful outcome without the use of laxatives (Category 1), successful outcome on laxatives (Category 2), failure to meet criteria for success on or off laxatives (Category 3).

Results: Long term outcome data were examined in 176 pts (95 M, 81 F; median age 5.9 yr, range 1.5 mo-20 yr). There was a psychiatric burden as pts developed depression (7.4%), anxiety (9.7%), or need for psychological therapy (19.3%). At 3 mo, 17.2% of pts met criteria for Category 1, 47.1% for Category 2, and 35.7% for Category 3. On unpaired t-test analysis, pts in Category 2 were older at biopsy (7.9 yr, p<0.01) with longer duration of constipation (4.1 yr, p<0.01) compared to Category 1 (1.2 yr and 0.9 yr respectively). Pts in Category 3 were also older at biopsy (8.3 yr, p<0.01) with longer duration of constipation (4.7 yr, p<0.01) compared to Category 1. At 2 yr, 15.4% of pts met criteria for Category 1, 50.0% for Category 2, and 34.6% for Category 3. On unpaired t-test analysis, pts in Category 3 had longer duration of constipation (5.3 yr, p<0.039) compared to Category 1 (2.3 yr) at biopsy.

Conclusions: A third of pts did not meet criteria for successful outcome with laxatives, while half required laxatives to achieve success. Younger age at biopsy and shorter duration of constipation prior to biopsy yielded greater chance at achieving successful outcome without laxatives. There is a prominent psychiatric burden in this population.

316 OUTCOME OF CHRONIC CONSTIPATED CHILDREN: 4-YEAR FOLLOW-UP STUDY. Marcia F. Torres, Pediatrics, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil
Marcia R. F. Torres1, Joseph F. G. Santos2, Isabela G. Ribeiro3, Aline S. Costa3, Barbara F. Gazzinelli3, Gabrielle Neves3, Marcella Costa3, Lais Campos3, Pedro Kaliil3, Maria do Carmo B. Melo1
1Gastroenterology, Hepatology and Nutrition Division of the Department of Pediatrics, School of Medicine and Hospital of Clinics, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil
2Epidemiologist, IPSEMG, BH, MG, Brazil, 3Graduate Student, School of Medicine, Federal University of Minas Gerais, BH, MG, Brazil

Goal: Longitudinal study of constipation after therapeutics and behavioral intervention.

Methods: Functional chronic constipated children, according to ROMA III criteria, were included in the follow-up study (approved by an ethical committee) at a tertiary ambulatory. At each follow-up appointment, general clinical aspects and aspects related to constipation were assessed.

Results: During almost four years, 202 consecutive constipated patients (53.5% male) (median age 5.4 years old) attended a university Pediatric Gastroenterology outpatient clinic and an extensive protocol was applied at each appointment. Among many data analyzed, we found that 29.7% (n=60) had one appointment, 20.3% (n=41) had two and 26.2% (n=53) had five. After intervention was made on the first appointment, significant improvement in the studied standards was detectable from the first to second appointments. Comparative analysis of the first and fifth appointments of 53 patients showed a significant reduction of large stool caliber rates, from 76.8% to 18.9% of patients [p=0.04]; stool retentive posture decreased from 60.4% to 37.8% [p=0001]; overflow fecal incontinence from 54% to 38.6% [p=0.001]; and fecal mass was present in 46.6% decreasing to 23.1%, respectively [p<0.001]. In the first appointment, 33.8% of patients reported toilet clogging episodes versus 11.5% by the fifth appointment. Fecal frequency of less than 3 times per week was found in 60.5% and 15.1% of patients in the first and fifth appointments of 53 patients showed significant reduction of large stool caliber rates, from 76.8% to 18.9% of patients [p=0.04]; stool retentive posture decreased from 60.4% to 37.8% [p=0001]; overflow fecal incontinence from 54% to 38.6% [p=0.001]; and fecal mass was present in 46.6% decreasing to 23.1%, respectively [p<0.001]. In the first appointment, 33.8% of patients reported toilet clogging episodes versus 11.5% by the fifth appointment. Fecal frequency of less than 3 times per week was found in 60.5% and 15.1% of patients in the first and fifth appointments, respectively [p<0.001].

Conclusion: Diagnostic and follow-up standards of constipation were improved after five follow-up appointments, more importantly after the first clinical intervention.

317 MOOD, SLEEP AND HPA REACTIVITY IN CHILDREN WITH ABDOMINAL PAIN: A COMPARISON BETWEEN OBJECTIVE AND SUBJECTIVE REPORTS. Sara E. Williams, Adrian Miranda
Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

Children with abdominal pain subjectively report more mood and sleep problems compared to well children; however, the degree to which objective measures of these factors differ between groups is not well established. The objective of the current study was to compare children with abdominal pain to well controls on subjective reports of anxiety, depression, and sleep, and objective measurements of sleep and HPA reactivity. Methods: 22 abdominal pain patients (68% female, 8-17 years old) and 20 well children (55% female, 8-17 years old) were recruited. Anxiety, depression, and subjective sleep questionnaires were completed. Three salivary cortisol measurements (waking, one hour after waking, evening) and one week of sleep actigraphy were recorded. Results: Pain patients
had greater anxiety (t=2.24, p<.05) and depression (t=2.34, p<.05) than controls, and adolescent pain patients reported more problems with sleep hygiene (t=3.60, p<.01) and sleep quality (t=2.95, p<.05) than adolescent controls. There were no differences between pain patients and controls on cortisol (at any time point or awakening response) or actigraphy (sleep time, awakenings, and efficiency). There were few significant correlations between subjective and objective measurements. Anxiety and depression were not significantly related to cortisol in either group. There were two significant correlations between objective and subjective sleep reports: controls with more sleep problems spent more time in bed (r=−.48, p=.05) and pain patients with more sleep problems had more nighttime awakenings (r=−.63, p<.05). Conclusions: Subjective anxiety, depression, and sleep ratings were significantly different between pain and controls, whereas objective measurements of sleep and HPA reactivity were not different between groups. There were few significant correlations between subjective and objective measures. Taken together, pain patients’ perceptions of their mood and sleep difficulties may not accurately reflect their physiological experience.

318 ARABIC TRANSLATION OF THE ROME III CRITERIA IS NOW AVAILABLE.
Eyad M. Altamimi, Mohammad Al Safadi, Pediatric, Mu'tah University, Alkarak, Jordan
Functional gastrointestinal disorders affect children of all ethnic groups. Rome criteria are symptom-based criteria allow a positive diagnosis of functional gastrointestinal disorders (FGIDS). The symptom based questionnaires are dependent on the understanding of the questions and expressions, which mandate these questionnaires being addressed in the patient’s language. As for Arabic speaking children there was no Arabic version of these questionnaires. This was depriving those children and their treating physicians from this very important diagnostic tool. So, we decided to translate the ROME III questionnaires into Arabic.

Method:
The Rome Foundation was contacted. Our interest in translating the criteria was expressed. The foundation permission was obtained. The process was performed according to the translation guidelines prepared by the foundation. The final validated Arabic version get the foundation recognition and approval by 12th of June,2012.

Discussion:
The major issues during the translation process were the cultural sensitivity of the topic and the availability of simple terms describing the symptoms. These problems were solved by using the predetermined standardized method of translation, the enthusiasm of the working team and the help of the foundation supervisor.

Conclusion:
We are so happy to denote that Arabic translation of ROME III criteria is now available for usage, through the Rome Foundation website at: http://www.romecriteria.org/translations/.

We believe this translation will be of tremendous value in diagnosis of (FGIDS) in Arabic speaking children.

NASPGHAN NEUROGASTROENTEROLOGY AND MOTILITY PRIZE
319* SALIVARY AMYLASE AS A BIOMARKER FOR FUNCTIONAL ABDOMINAL PAIN IN CHILDREN: ROLE OF SLEEP AND MELATONIN. Adrian Miranda1, Hershel Raff1,1, Sara E. Williams1
1Medical College of Wisconsin, Milwaukee, WI, WI; 2Aurora St. Luke’s Medical Center, Milwaukee, WI
Introduction: Effective treatments and biomarkers are lacking in children with functional gastrointestinal disorders (FGIDs). We investigated the anti-nociceptive properties of melatonin in children with abdominal pain and examined changes in salivary alpha-amylase (sAA), pain, sleep, and mood. Methods: FGID patients (n=17) and age matched controls (n=19) were recruited (ages 8-17). In all groups, abdominal pain (API), mood (RCADS), and pain catastrophizing (PCS) questionnaires were administered. Measures of sAA were collected at 0600, 0700 and 2200 and actigraphy was recorded for 7 days. Abdominal pain ratings were recorded with a daily diary and twice daily with actiwatch. Following baseline data collection in the FGID group, melatonin (3mg/d, age<13y/o or 6mg/d, age≥13y/o) was given for 5 weeks. At the end of treatment, sAA measures, actigraphy and questionnaires were repeated. Results: 51% in the FGID group had significant improvement in abdominal pain in all 3 measures post-melatonin. There was at least a 32% improvement in overall pain in daily diary (4.17 to 2.87) and actiwatch scores (3.06 to 1.81) (p<0.05). Marked improvement in API scores was also noted (6.44 to 4.83, p<0.05). FGID patients at baseline, had a significantly greater sAA awakening response compared to controls (14.59 and -1.61, respectively, p=0.047). Evening sAA was also significantly higher in the FGID group (39.4 and 17.4 U/ml, p=0.008). There was a trend towards an attenuation of the sAA awakening response following melatonin treatment in FGID patients (16 and 0.71, p=.095). Melatonin treatment did not affect any of the psychological measures. Sleep parameters (average sleep time, awakening and efficiency) were no different from controls at baseline or following melatonin treatment.

Conclusion: There is a marked increase in sAA levels in children with pain associated-FGID compared to healthy children, indicating a difference in adrenergic activation. Melatonin improves abdominal pain in children without affecting sleep, mood, or catastrophizing.
Hepatobiliary/Transplant

323 A POPULATION-BASED STUDY OF PEDIATRIC PRIMARY SCLEROSING CHOLANGITIS/INFLAMMATORY BOWEL DISEASE IN UTAH. Mark Deneau1, M. Kyle Jensen1, John Holmen2, Marc Williams2, Steven Bleyl2, Stephen Guthery1, 1University of Utah, Salt Lake City, UT; 2Intermountain Healthcare, Salt Lake City, UT

Introduction: Primary sclerosing cholangitis (PSC) is an immune-mediated extraintestinal manifestation of inflammatory bowel disease (IBD). There are few population-based studies of PSC-IBD in children.

Methods: The majority of adult gastroenterologists, all pediatric gastroenterologists, and all transplant hepatologists practice within two Utah hospital systems that constitute a catchment area covering the entire state. We reviewed the electronic medical records of 1,224 pediatric patients from both systems with at least one encounter associated with an ICD-9 code for IBD between January 1, 2005 and December 31, 2011. We used standard criteria for the diagnosis of ulcerative colitis (UC) and Crohn's disease (CD). We used laboratory, histology, and cholangiography data for the diagnosis of PSC. We calculated prevalence and incidence using US Census data. We additionally constructed a retrospective cohort of PSC-IBD patients and followed them to endpoints of death or liver transplantation.

Results: We identified 605 pediatric patients with IBD. PSC was identified in 34 (5.6%). Overall, 10.5% of UC patients and 1.3% of CD patients were diagnosed with PSC. 9 patients (26.5%) had overlap with autoimmune hepatitis. The incidence and prevalence of pediatric IBD and IBD-PSC in Utah are 5.7 and 22.3, and 0.2 and 0.9 per 100,000 children, respectively. 5-year survival with native liver after diagnosis of PSC was 80% (95% CI 61-91%). Patients had a mean of 3.9 years of follow-up data available. Two IBD-PSC patients (5.9%) developed cholangiocarcinoma.

Conclusions: PSC occurred at a greater frequency in pediatric IBD than previously reported. A significant number of PSC-IBD patients require liver transplantation within 5 years of their diagnosis. Cholangiocarcinoma is a rare but life-threatening complication in this population. Incidence and prevalence estimates for Crohn disease and ulcerative colitis largely mirror those previously reported, indicating near complete sampling of pediatric IBD patients in Utah.

324 CLINICAL, BIOCHEMICAL AND HISTOLOGICAL CHARACTERISTICS OF PATIENTS WITH AUTOIMMUNE HEPATITIS. Edith Gonzalez, Bojorquez Maria del Carmen, Guillermima Gomez Gastroenterology and Nutrition Pediatric, CMNO Hospital of Pediatric IMSS, Guadalajara, Mexico

Objectives: To establish the clinical and biochemical behavior at the time of diagnosis as well as the histological findings in our population with Autoimmune Hepatitis (AIH).

Patients and methods: In this cross-sectional study we included children diagnosed with AIH, younger than 16 years old, from January 2001 to December 2011, both outpatients and hospitalized, who fulfilled the criteria published by the AHIG in 1999 and had their medical records complete from the time of diagnosis. In selected patients, the clinical course of the disease at presentation as well as the biochemical and histological findings were identified. In order to determine the degree of liver damage we also calculated the Child-Pugh, Malatak and PELD scores in each patient.

Results and discussion: We studied 25 patients, 64% of which were female and had an average age of 8 years 7 months ± 47.62. The most frequent form of clinical presentation was acute hepatitis, which occurred in 14 patients (56%) with an average of 10.05 months from the time of beginning of symptoms to the time diagnosis was made. The totality of patients had biochemical alterations, being the transaminases' elevation the most frequent one, with a marked elevation of the AST over the ALT. Also, hypergammaglobulinemia was identified in 94% of cases. Liver biopsy was performed in 96% of cases at time of diagnosis and 100% of these had interface hepatitis as well as fibrosis. The average Child-Pugh score was 6.1 ± 1.92 and 13.62 ± 13.77 for the Malatak score. The average PELD score was 2.00 ± 9.57 and for the MELD score was 9.8 ± 3.11.

Conclusions: AIH is more frequent in the female gender however its presentation in male patients is not rare. Two thirds of the AIH patients were classified as stage A in the Child-Pugh score, this fact as well as its initial presentation being in the form of acute hepatitis with a prolonged clinical course demands a high clinical suspicion from the pediatrician in order to achieve an opportune reference as well as an adequate and opportune diagnosis and treatment.

325 A POTENTIALLY FATAL EVENT ASSOCIATED WITH PEGYLATED INTERFERON AND RIBAVIRIN THERAPY IN A CHILD WITH CHRONIC HEPATITIS C. Susan Hilk1, James Howard2, Arup Roy-Burman2, Dane Gehringer2, Rose Ellen Morrell2, Gregory Enns2, Carol Brosgrist1, Paul Harmatz3

1Children's Hospital Oakland, Oakland, CA; 2UCSF, San Francisco, CA; 3Stanford University, Palo Alto, CA

Treatment of chronic hepatitis C virus (HCV) infection through combination therapy with pegylated interferon alpha-2a or -2b (PEG-IFN) and ribavirin (RBV) is an effective strategy for obtaining a sustained virological response. This has correlated with significant improvement in clinical outcomes. Combination therapy with PEG-IFN/RBV was approved for use in children 3 to 17 years old in 2008. We present the first described, life-threatening severe adverse event in an otherwise healthy 5 year old white, non-Hispanic male with vertically acquired genotype
3a HCV. Within 24 hours of his initial therapeutic dose (60 mcg/m2 of subcutaneous PEG-IFN alpha-2b, followed by 7.5 mg/kg oral RBV), the patient developed vasopressor dependent shock with minimal oxygen extraction, extreme neurological impairment, and multi-organ dysfunction including respiratory failure, massive polyuria, and acute transaminits. No evidence of bacterial, fungal or acute viral infections. His near fatal condition began to slowly improve four days after onset, after discontinuation of antibiotics. With the exception of elevated serum lactate levels, general screens for metabolic disorders and potentially toxic drugs (including acetaminophen) were negative during the acute phase of his illness. The episode was reported to the USFDA. Medication lots were evaluated by the manufacturer (Schering), but no abnormalities were found. Fibroblasts generated from skin biopsy tested negative for inherent deficiencies in electron transport chain complexes I-IV. Specific testing for abnormalities in candidate mitochondrial genes remains underway. Although the patient's initial condition was extremely grave, he was successfully weaned from supportive care. No major sequelae have been noted in close follow-up. Overall, his course was consistent with an acute mitochondrial toxicity, although the exact nature remains elusive.

326 BREAST FEEDING IS BETTER THAN FORMULA FEEDING IN PREVENTING PARENTERAL NUTRITION ASSOCIATED LIVER DISEASE IN INFANTS ON PROLONGED PARENTERAL NUTRITION. Sakil S. Kulkarni¹, Velma Mercado², Mirta Rios Rios², Roberto Gomara³, Luis Caicedo³, William Muinos³, Jesse Reeves-Garcia³, Erick Hernandez³, ¹Medical Education, Miami Children's Hospital, Miami, FL; ²Clinical Nutrition, Miami Children's Hospital, Miami, FL; ³Pediatric Gastroenterology, Miami Children's Hospital, Miami, FL

Parenteral Nutrition associated liver dysfunction (PNALD) is common in infants receiving prolong parenteral nutrition. Breast milk or amino acid formulas are shown to be associated with greater success with regards to weaning from parenteral nutrition in children with intestinal failure. But there are only a few studies investigating the role of breast milk in decreasing PNALD. Our aim is to investigate if breast milk is superior to infant formulas in preventing PNALD.

We conducted a retrospective analysis of 79 newborns requiring parenteral nutrition for more than two weeks. They were divided into three different groups (exclusive breast feeding, exclusive formula feeding and mixed feeding). We analyzed and compared the levels of bilirubin, liver enzymes, total days on parenteral nutrition, episodes of sepsis, albumin, and C reactive protein level amongst the three groups.

We found that the infants who were exclusively breastfeed (33.3%) were significantly less likely to develop PNALD compared to those who were fed only formula milk (70.4%) \(p = 0.005\). Also the incidence of PNALD in the infants who received mixed feeding (both breast and formula) (45.5%) was significantly less than those who were fed only formula milk (70.4%) \(p = 0.05\) . There was no significant difference between the exclusive breast feeding and mixed feeding groups. Also, the mean maximum direct bilirubin \(p = 0.02\) as well as the mean maximum AST were significantly lower in the breast feeding group \(p = 0.04\) compared to the formula group. The mean number of days on TPN in the two groups were not significantly different \(p = 0.654\).

Breast milk as a modality for early enteral nutrition may be protective against the development of PNALD, independent of the duration of parenteral nutrition.

327 PRACTICE VARIATION IN PEDIATRIC AUTOIMMUNE HEPATITIS (AIH). Paul Maloney¹, Najma Ahmed², Jeff Critch¹, ¹Memorial University, St. John's, NF, Canada; ²Gastroenterology, McGill University, Montreal, QC, Canada

Aim: To assess the management of pediatric AIH among NASPGHAN members. Methods: An internet survey was emailed to members in April 2011. Responses were anonymous. Results: 218 responses were obtained from 1594 delivered surveys (14%). Most members perform the same diagnostic tests. Despite the possibility of overlap syndromes, only 14% routinely perform MRCP. Considerable variation exists in management. For induction, 46% use 1mg/kg of prednisone and 48% use 2mg/kg. 35% initiate prednisone wean after a specific time and 56% initiate wean based on reduction in transaminase levels. 43% wean prednisone over 1-3m, 18% in 4-6m, and 7% >6m. 8% wean prednisone to 10mg/d, 16% to 5mg/d, 6% to 2.5mg/d, 5% to 10mg/qod, 5% to 2.5mg/qod and 23% wean off. For type I, 64% routinely use azathioprine in treatment and 16% only if incomplete steroid response (similar for type II). 70% routinely assess TPMT activity. 49% monitor 6TG levels. 32% initiate azathioprine at 1mg/kg, 10% at 1.5mg/kg, 10% at 2mg/kg and 29% based on TPMT. For type I maintenance, 3% never discontinue prednisone to use azathioprine monotherapy, 56% will discontinue prednisone soon after transaminases normalize (<1y), 21% if normal transaminases for 1-2 years, 5% if normal transaminases for 2-3y, and 3% if normal transaminases for more than 3 years (similar for type II). To be considered in remission, 50%
require complete clinical recovery, 90% normal transaminases, 24% normal IgG, 19% ANA ≤ 1:40, 41% histological resolution of inflammation. For type I, 0.5% discontinue maintenance if in remission for ≤ 1y, 21% 1-2y, 27% 2-3y, 19% >3y, 21% never discontinue. 13% do not routinely do a followup liver biopsy, 54% biopsy before stopping maintenance, and 6% after stopping maintenance (similar for type II). Stratification based on academic versus non-academic practice and years in practice did not change the results. Conclusions: Greater variation exists in the management of pediatric AIH than in the diagnostic workup likely related to limited data from longterm RCTs. Practices may differ in members not taking the survey.

328 USE OF IMMUNOHISTOCHEMISTRY TO IDENTIFY AND TREAT A NOVEL CD8-MEDIATED CAUSE OF ACUTE HEPATITIS IN CHILDREN. Rebecca B. McKenzie, William Berquist, Kari Nadeau, Sharon Chen, Richard Sibley, Kenneth Cox, Stanford University, Palo Alto, CA

Introduction: Routine evaluation fails to identify a cause for acute liver failure in 50% of children. In a case series of 3 patients with acute hepatitis, immunohistochemical staining of liver tissue was used to identify and treat atypical immune-mediated causes of acute liver injury. Methods: Laboratory screening for genetic, metabolic, autoimmune (IgG, ANA, Anti-LK, Anti-Sm) and infectious studies from blood and tissue were performed. Liver biopsies were stained by the Stanford Immunoperoxidase Laboratory for antibodies to CD3/4/8/20/56/138 and 163. Viral PCR and staining for EBV, CMV, parvovirus and adenovirus was conducted as appropriate. Results: All patients presented with baseline AST and ALT (1959-4700), T bili (7.8-14.5), INR (1.2-1.5). Genetic, metabolic and autoimmune markers were negative. One patient had an elevated IgG level. All patients were male and ages 2-11. Infectious studies including serology for EBV, CMV, Hepatitis A-C were negative for acute infection. Liver biopsy showed acute hepatitis with predominance of cytotoxic CD8 T-cells and paucity of CD4 and CD20 B-cells. All were treated with 0.4 gm/kg of IVIG, 2 mg/kg of solumedrol (maximum dose 60 mg) followed by a prednisone taper. In all cases, AST and ALT decreased to 50% at 48 hours and normalized by 1-2 months in 2 patients. Case 3 has near normal values at 1 month. Total bilirubin normalized by 1 month and INR by 2-6 days in all cases. No patient developed liver failure or underwent liver transplantation. Conclusions: Immunohistochemical staining successfully identified a novel, CD8 T-cell mediated autoimmune/inflammatory cause of acute hepatitis. These atypical cases in male children were missed by routine clinical evaluation but responded to immunomodulator therapy and normalized hepatic function. Further studies are needed to better identify these atypical cases that may otherwise progress to liver failure and require transplantation if left untreated.

329 FULMINANT HEPATIC FAILURE IN MEXICAN CHILDREN: ETIOLOGY AND PREDICTORS OF MORTALITY. Ericka B. Montijo, Ana Lisa O. Sanchez, Jaime M. Ramirez, Roberto B. Cervantes, Flora M. Zarate, Jose L. Cadena, Monserrat M. Cazarez, Erick M. Toro, Gastroenterology, Instituto Nacional de Pediatría, Naucalpan, Mexico

Fulminant hepatic failure (FHF) is a clinical syndrome developing as a result of massive cell necrosis occurring in patients without preexisting liver disease with a high mortality rate in the absence of liver transplantation. The majority of studies on FHF were conducted in Europe, EUA and Japan; there are no reported studies from Mexico. Common etiologic factors in develop countries include paracetamol overdose, idiosyncratic drug reactions, hepatitis B virus infection; in Mexico the principal cause is hepatitis A virus infection. Prognoses features are suggested in pediatric patients from develop countries but not in developing.

The aim was to study the etiology, outcome and prognostic indicators in children with fulminant hepatic failure. DESIGN: This is a retrospective case and controls study, in 70 pediatric patients presenting in the Instituto Nacional de Pediatría in Mexico City, with fulminant hepatis failure, from January 2001 to August 2011. FHF was defined as presence of coagulopathy with or without encephalopathy within 8 weeks of the onset of symptoms. RESULTS: 70 children (33 male, 37 female, median age 56 (43-70)) were identified with FHF. The etiologies were 37 infectious, 6 metabolic, 1 drug induced (paracetamol), 12 autoimmune and 10 idiopathic. The most frequent infection was Hepatitis A virus infection. Prognoses features are suggested in pediatric patients from develop countries but not in developing.

The survival rate was 70%. The level of Hepatic encephalopathy result in a prognosis factor: Level 1-2 vs. 3-4 77%(survival) vs 8.3%; p<0.001; presence of digestive hemorrhage 28% (survival patients) versus 66% (p 0.0029); higher prothrombin time 46.6 vs. 29.5 (survival) p 0.0022, INR 4.52 vs 2.84 (survival patients) p 0.0006; higher plasma bilirubin 21.3 vs. 14.5mg/dL (survival patient) p 0.0145; higher ammonium levels 174 vs. 80 (survival patients) p <0.0001.

CONCLUSIONS: In developing countries Hepatitis A virus is the most frecuent cause of HFH. Children with FHF with severe coagulopathy, digestive hemorrhage, higher plasma bilirrubin, ammonium and white blood cells have a bag prognosis.
330 PEDIATRIC PERCUTANEOUS LIVER BIOPSIES (PLB) - 10 YEAR OUTCOMES. Khiet D. Ngo, Emily Whang, Amul Shah, Marquelle Klooster, George Tami, Trinh Truong, Manoj Shah, Pediatrics, Loma Linda University School of Medicine, Loma Linda, CA

AIM: Describe the outcomes of PLB at a single academic children's hospital.

METHOD: Retrospective review of patients <18y.o. Demographic and clinical data were extracted and analyzed using SPSS ® (v18). Independent t-tests and chi-square tests were used to analyze continuous and categorical variables respectively. P-values of <0.05 were considered statistically significant. All PLB were performed using the right intercostal approach with either the Jamshidi or Bard devices. Midazolam and ketamine were used for sedation in most cases.

RESULTS: From 2001-2011 365 PLB were performed in 323 patients. Mean age=7.7yr (2mo-18yr). Mean weight=33.8kg (2-135kg). Females=187. Outpatient biopsies=158. Indication:133 hepatitis/hyperbilirubinemia, 37 suspected transplant rejection, 22 follow-up for chronic transfusions, 62 follow-up of known liver disease, 6 others. Ultrasound guidance was used in 154 cases. Overall complication rate=8.5% (n=31). 27 complications occurred in hospitalized patients. 1.9% of complications were of major significance (hemotorax, sepsis, liver laceration, splenic laceration, reduction in hemoglobin needing transfusion, clinical decompensation), 2.7% of intermediate significance (inadequate sampling, incidental renal biopsy) and 3.8% were of minor significance (hemoglobin reduction not requiring transfusion, vomiting, abdominal pain, transient oxygen desaturation). Statistically significant predictors of complications included: hospitalized patients (p<0.001), lower weight (p=0.008), and greater post-procedure %hemoglobin change (p=0.024). Statistically insignificant predictors of complications included: pre-procedure INR/platelet/hemoglobin, mg/kg of midazolam and ketamine, usage of ultrasound guidance, number of needle insertions, gender, and age. While age did not reach statistical significance, 19 of the 31 complications were in patients <2yr.

CONCLUSIONS: Outpatient PLB in children is generally a safe procedure. Patients who are hospitalized, smaller, and have larger post-procedure %hemoglobin change are at greater risk for complications.

331 CORRELATION OF GALLBLADDER EJECTION FRACTION WITH DEGREE OF CHOLECYSTITIS IN CHILDREN UNDERGOING CHOLECYSTECTOMY. Ajay Rana1, Guilian Niu2, Maroun Karam3, Dave Jones2, Cary M. Qualia1, 1Pediatrics, Albany Medical Center, Albany, NY; 2Pathology, Albany Medical Center, Albany, NY; 3Nuclear Medicine, Albany Medical Center, Albany, NY

Objective: Children suspected of having acalculous cholecystitis or biliary dyskinesia often undergo 99mTc-cholestochinodiacetic acid cholescintigraphy with cholecystokinin (CCK HIDA) in order to determine gallbladder ejection fraction (EF) prior to cholecystectomy. A retrospective analysis was conducted in an attempt to determine whether EF correlates with degree of cholecystitis. Methods: Children 18 years and younger who had undergone cholecystectomies at Albany Medical Center between the years of 2009 and 2011 were identified. For those children who had also undergone CCK HIDA, the calculated EF was recorded. An EF<35% was considered abnormal. A grading scale adapted from Kasprzak et al. (Pol J Pathol, 2011) was used to determine degree of cholecystitis (Grade 0 to 6, where 0=no inflammatory cells and 6=most intense inflammation). Results: 22 cholecystectomies were performed on children during the above study period. The most common indication for surgery was abdominal pain. The age range of the patients was 6 to 16 years (mean age=13.8 years). Of the children undergoing cholecystectomy, gallbladder EF was determined for 16 patients. The mean EF was 28% (range=9 to 87%). The EF was not significantly related to the degree of inflammation (Analysis of variance, p=0.64). Of note, the 4 patients with normal EF all had Grade 3 or 4 cholecystitis and the one patient no with inflammation had an abnormal EF of 27%. Conclusions: This small observational study suggests that gallbladder ejection fraction cannot be used to predict the degree of cholecystitis in children. A larger number of subjects would be needed to confirm this finding.

332 HEPATITIS B VIRUS IN COLOMBIAN CHILDREN WITH HIV/AIDS. Carlos A. Velasco-Benitez1, Matira P. Sanchez2, Pio Lopez4, 1Universidad del Valle, Cali, Colombia; 4Fundacion Valle del Lili, Cali, Colombia

Introduction: In children with HIV/AIDS after vaccination for hepatitis B virus (HBV) seroconversion is low associated factor was the temporal relationship between the last dose of vaccination and the onset of treatment for 0-3 years (OR = 4.3 95%CI 0.96 to 19.23 p = 0.056) and > 3 years (OR = 9.69 95%CI 2.37-39.5% p = 0.002).

Conclusion: One third of patients seroconverted, and it was found associated with the temporal relationship between initiation of treatment and last dose of vaccine
**333 EVALUATION GUIDELINES FOR SUSPECTED MITOCHONDRIAL HEPATOPATHIES.**


**Background and Aims:** Mitochondrial hepatopathies (MITOHEP) can present in infancy or later, with acute liver failure (ALF) or chronic liver disease (CLD). Available genetic testing for new syndromes is increasing. The MITOHEP study group, a sub-group of the CHILDREN Research Consortium, prepared a guideline for the evaluation of children suspected of having these complex disorders.

**Methods:** The MITOHEP Committee, pediatric hepatologists and a mitochondrial metabolism expert, outlined a tiered approach to evaluation using Medline searches and the group's expertise; a table detailing clinical features and diagnostic testing was designed.

**Results:** Evaluation of the child with suspected mitochondrial disease (ALF, CLD with steatohepatitis, hypoglycemia, or acidosis, or liver disease accompanied by multisystem involvement) was outlined:

- **Tier 1:** Screening tests of blood and urine that might indicate potential underlying mitochondrial disease: comprehensive metabolic profile, CPK, phosphorus, lactate/pyruvate, ketone bodies, acylcarnitine profile, urine organic acids, serum amino acids.
- **Tier 2:** Genotyping for more common mitochondrial disease-causing genes or those with specific diagnostic clues; POLG, DGUOK, and MPV17 are the most common.
- **Tier 3:** Evaluation of liver, skin, and muscle: histology, enzymology and genetic studies.
- **Tier 4:** Further molecular and biochemical evaluation including additional genotyping.

Evaluation for disease in other organ systems when liver transplant is being considered was specified: CNS, cardiovascular, renal, ophthalmologic, endocrine and pancreatic studies. Optimal management of the child during testing may decrease risk of iatrogenic complications.

A Table describing each syndrome, molecular defect, gene, onset, hepatic presentation, neurologic presentation/other features and diagnostic tests was prepared (will be presented in poster).

**Conclusion:** The clinician can use a systematic approach to negotiate a complex and growing body of knowledge to effectively assess the child with suspected mitochondrial liver disease.

---

**334 HIGH PREVALENCE OF AUTOANTIBODY (AUTOAB) POSITIVITY IN CHILDREN WITH PEDIATRIC ACUTE LIVER FAILURE (PALF).**

Michael Narkewicz1, V. Ng2, R. Romero1, S. Horslen1, D. Rudnick3, S. Zhang4, S. Belle7, R. Squires6, 1Univ of CO, Aurora, CO; 2Hosp for Sick Children, Toronto, ON, Canada; 3Emory Univ, Atlanta, GA; 4Univ Wash, Seattle, WA; 5Wash Univ, St Louis, MO; 6Children's Hosp, Pittsburgh, PA; 7Univ of Pitts, Pittsburgh, PA

Screening by autoantibodies (autoAB) is common in a search for a treatable cause of ALF in children. The purpose of this study was to determine the frequency, clinical characteristics and outcome of participants in the PALF study according to ANA, anti-smooth muscle AB (ASMA) and anti-liver-kidney microsomal AB (ALKM) status.

**Methods:** Subjects enrolled in the PALF study were eligible. ANA, ASMA, ALKM were determined at clinical labs (n=622) or stored serum (n=316) at a central lab. In 216, both lab results were available. ANA ≥ 1:80, ASMA and ALKM ≥ 1:40 were considered positive (+).

**Results:** Between 1999 and 2010, 986 subjects were enrolled in PALF. AutoAB results were available on 722 (73.2%) with 203 (28.1%) AutoAB+. The final investigator assigned diagnoses for autoAB + subjects were: AIH (63), Indeterminate (76), Other known diagnoses (64: with 19 metabolic disease (12 Wilson, 7 other), 12 viral infection, 9 APAP and 24 other diagnoses). AutoAB were more common in Wilson (12/32, 37%) vs other known diagnoses (52/253, 20.6%, p=0.03). ALKM + subjects were younger (median 2.7 yrs vs 9.1 yrs p=0.0003) and tended to be more likely to receive a liver transplant (51.6% vs 31.4% p=0.06) than other autoAB+, after adjusting for age. This was similar if all acetaminophen (APAP) subjects were excluded. In those with indeterminate PALF, a larger percent of AutoAB+ were female (55%) than were female among AutoAB- (42%) (p=0.03).

**Conclusions:** Positive AutoAB occurs in at least 28% of children with PALF and occurred across final diagnostic categories. PALF participants without APAP and at least one AutoAB+ have similar outcomes to AutoAB negative (non-APAP). However, ALKM children with PALF are younger and tended to be more likely to receive OLT compared to other AutoAB+ and AutoAB negative (non-APAP) patients. The significance of AutoAB+ PALF remains uncertain.

---

**335 PEGYLATED INTERFERON α2B (PEG-IFN2B) IN CHILDREN WITH HEPATITIS C AND KIDNEY FAILURE.**

Rocío Macías-Rosales1, Alfredo Larrosa-Haro2, Sergio Pacheco-Sotelo1, 1Gastroenterology and Nutrition, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Centro Universitario en Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

**AIM:** To assess the response to treatment with PEG-IFNα2b monotherapy in children with hepatitis C and kidney failure.

**CASE REPORT:** Two teenagers with chronic renal failure on hemodialysis, renal transplant protocol and hepatitis C
are reported. Genotype was 1a, viral load was >700,000IU/mL and transferases were increased. HIV and HBV infection were ruled out; thyroid profile, serum immunoglobulins and alpha-fetoprotein were normal. In one, liver biopsy showed portal fibrosis, scarce septa (F2) and minimal activity (A1), with METAVIR index of 3; in the other patient there was not fibrosis (F0), and the activity was minimal (A1), METAVIR was 1. PEG-IFN2α was initiated, 1 µg/kg subcutaneously every week for 1 year. Transferases normalized after 3 weeks and viral load was <43 IU/mL at 3 and until 12 months of treatment. Both patients had fever and myalgia; leukocyte, platelet and neutrophil count was normal along the trial and hemoglobin decreased in one patient, 3 months before the end of treatment. At the end-point of treatment, HIV, HBV, thyroid profile, immunoglobulins, alpha-fetoprotein, and ultrasonography were all within normal limits.

CONCLUSION: Treatment of our patients with PEG-IFN2α as monotherapy was effective to control viral load and to improve liver damage without significant adverse effects.

336 CYSTIC FIBROSIS LIVER DISEASE REDUCES SURVIVAL IN PATIENTS WITH CYSTIC FIBROSIS. Billy Bourke1,2, Marion Rowland1,2, Cliona Gallagher1,2, Charles Gallagher3, Risteard O’Laoid3, Gerard Canny1, Annemarie Broderick1, Peter Greally4, Dubhfeasa Slattery3, Leslie Daly6, Noel G. McElvaney7
1Gastroenterology, Our Ladys Childrens Hospital, University College Dublin, Dublin, Ireland; 2School of Medicine and Medical Science, UCD, Dublin, Ireland; 3St Vincents University Hospital, UCD, Dublin, Ireland; 4National Children Hospital, Dublin, Ireland; 5Childrens University Hospital, Dublin, Ireland; 6School of Public Health, UCD, Dublin, Ireland; 7Beaumont Hospital, RCSI, Dublin, Ireland

BACKGROUND: With improvement in pulmonary treatments patients with cystic fibrosis (CF) are surviving longer and less common manifestation such as CF liver disease (CFLD) assume increasing importance. We aimed to determine if CFLD was a risk factor for mortality in CF.

METHODS: In 2000 we recruited all children with CFLD in Ireland and compared them to age and gender matched children with CF and no evidence of liver disease (1). In this study we compare the 10 year mortality between these two groups.

RESULTS: Seventy two of 84 (85.7%) of the original participants were eligible for follow-up, (mean age CFLD participants 21.71yrs SD6.50, CF controls 23.6 SD5.6). Patients with liver disease had a significantly increased mortality (38.9%; 14/36) compared with those without liver involvement (13.9%; 5/36 (odds ratio 3.9 95%CI 1.2-12.6 p=0.005). The risk for death was higher in females with liver disease (9/14; 64.3%) compared with males (5/22; 22.7%), (OR 5.7 95%CI 1.3-28.2), despite there being more males with liver disease than females in the cohort. In a logistic regression model, liver disease (OR 4.3 95%CI 1.07-17.16) female gender (OR 12.3 95%CI 2.4-63.2), reduced pulmonary function, (FEV1% predicted Z score <-2SD) (OR 5.1 95%CI 1.1-23.8) each were independent risk factors for mortality in CF.

CONCLUSIONS: The presence of clinically significant liver involvement is a marker of worse outcome in CF. Females with liver disease are at increased risk of mortality compared to males.

337 THE ROLE OF LIVER BIOPSY IN THE DIAGNOSIS OF FOCAL NODULAR HYPERPLASIA IN CHILDREN. Pamela L. Valentino1,2, Simon C. Ling1,2, Vicky L. Ng1,2, Philip John3, Binita M. Kamath1,2
1Div of GI, Hepatology & Nutrition, Hospital for Sick Children, Toronto, ON, Canada; 2Dept of Pediatrics, University of Toronto, Toronto, ON, Canada; 3Interventional Radiology & Diagnostic Imaging, Hospital for Sick Children, Toronto, ON, Canada

Focal nodular hyperplasia (FNH) is a benign liver tumor with a characteristic appearance on imaging and histology that is managed conservatively. The differential diagnosis includes malignancy, such as fibrolamellar hepatocellular carcinoma (fHCC). We sought to determine the diagnostic accuracy of imaging for FNH in children without comorbidities, as compared to liver biopsy.

Methods: 304 consecutive patients referred with a liver mass at <18 years that underwent biopsy were retrospectively ascertained (1990-2010). Cases with a history of malignancy, liver disease or transplant, or underlying syndromes were excluded. Imaging & histology reports were reviewed.

Results: After excluding 205 cases, 99 were studied. The most common histological diagnosis was hepatoblastoma (46%). 23 cases of FNH were found in children without comorbidities. Their mean age at diagnosis was 11.1±5.2years, were followed for 2.6±1.2years and the majority were female (78%). Of these, 19 met standard criteria for FNH on both imaging and histopathology. In 4 cases of biopsy-proven FNH, imaging did not suggest FNH. The sensitivity of diagnostic imaging for FNH was MRI:87% (13/15), CT:71% (10/14) and US:63% (12/19cases). All children whose imaging suspected FNH had this diagnosis confirmed on histology, except for 2 cases: hepatocellular adenoma (CT&US,2003) and fHCC (MRI,1993). Imaging performance for FNH was: sensitivity 83%, specificity 97%, PPV 91%, and NPV 95%.
Conclusions: In this cohort of children with liver mass and no co-morbidities, a diagnosis of FNH by imaging was highly specific, despite 1 case of malignancy mistaken for FNH based on low-quality imaging. MRI is more sensitive than US/CT for diagnosis of FNH. A liver biopsy may be deferred in a healthy, non-comorbid, child with a liver mass, whose evaluation, including MRI imaging, is classical for FNH. Our practice is to repeat imaging within 3-6mo initially.

338* INCREASED PHOSPHORYLATION OF MTOR DURING ISCHEMIA REPERFUSION INJURY IN FATTY LIVER IS MITIGATED BY GLP-1R AGONIST EXENDIN4 LEADING TO LIPOLYSIS. Vasantha L. Kolachala1, Rong Jiang1, Carlos Abramowsky2,3, Allan Kirk2,4, Nitika A. Gupta1,2, 1Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; 2Transplant Services, Childrens Healthcare of Atlanta, Atlanta, GA; 3Department of Pathology, Emory University School of Medicine, Atlanta, GA; 4Department of Surgery, Emory University School of Medicine, Atlanta, GA

Background: Ischemia reperfusion injury (IRI) is a common clinical scenario. With the rising incidence of fatty liver disease, a large proportion of livers undergoing IRI are steatotic. We have shown that Ex4, a GLP-1R agonist decreases hepatic steatosis and mitigates cell death after IRI but the underlying mechanism for this action remains elusive. Mammalian target of rapamycin (mTOR) pathway is a diverse pathway involved in lipolysis, energy balance and ischemic stress. Aim: To identify the underlying mechanism of action of Ex4 in protection against IRI and stimulation of lipolysis by exploring the mTOR pathway. Methods: C57BL/6 mice were fed a high fat diet (HFD) and subjected to IRI with Ex4 treatment. In addition, HuH 7 cells were made steatotic and exposed to hypoxia/ischemia/reperfusion and exposed to Ex4. Triglyceride levels, phosphorylation of mTOR and hormone sensitive lipase (HSL) were assessed. Exendin9-39 was used an inhibitor of GLP-1signaling. Results: Increased phosphorylation of mTOR was seen in HFD mice subjected to IRI. On treatment with Ex4, this was significantly reduced (0.05±0.006 vs 0.12±0.01 RDU; p<0.001). A similar trend was observed with total mTOR (0.4±0.01 vs 0.8±0.06 RDU; p<0.01). Steatotic HuH7 cells subjected to hypoxia/ischemia/ reperfusion also demonstrated increased phosphorylated and total mTOR compared to non steatotic cells, which was mitigated by Ex4 (p<0.003 & p<0.01 respectively). Pre-treatment with Ex9-39 abolished this effect, leading to increased phosphorylated and total mTOR (p<0.01). Additionally, Ex4 treatment led to increased phophorylation of HSL and decreased triglyceride content in steatotic hepatocytes, both of which are hallmarks of lipolysis. Conclusion: Exendin 4 acts by inhibiting the mTOR pathway and stimulating lipolysis which in turn protects steatotic cells from IRI related cell death. Hence we postulate that the mTOR pathway may be the critical underlying signaling pathway involved in reduction of cell death and activation of lipolysis by Ex4.

339 MODULATION OF ATAXIA TELANGIECTASIA MUTATED (ATM) PATHWAYS REVERSES ACETAMINOPHEN (APAP)-INDUCED HEPATOTOXICITY WITH ACUTE LIVER FAILURE (ALF). Preeti Viswanathan1, Sriram Bandi2, Sanjeev Gupta1, 1Pediatric Gastroenterology and Hepatology, Childrens Hospital at Montefiore, Albert Einstein college of Medicine, Bronx, NY; 2Medicine and Pathology, Marion Bessin Liver Research Centre, Albert Einstein College of Medicine, Bronx, NY

The ATM signaling pathway protects cellular DNA integrity. We found APAP caused hepatic DNA damage with activation of ATM pathways. In C57BL/6 mice given LD50 dose of APAP, we observed encephalopathy, abnormal liver tests, liver necrosis, and mortalities. Real-time RT-PCR for 252 relevant genes showed oxidative stress, inflammation, and altered expression of ATM pathway genes, including DNA damage/repair and cell cycle regulators. H2AX staining confirmed oxidative DNA damage and Comet assays revealed DNA strand breaks, which are typical effects of low ATM expression. The findings were replicated in Huh7 human hepatocytes. Moreover, regulation of ATM signaling by APAP was verified in genetically-engineered Huh7 cells expressing human ATM promoter reporter. Next, to advance therapeutic development in this context of ATM dysregulation, we studied G-CSF, which was known to regulate ATM promoter. G-CSF restored ATM promoter activity in Huh7 cells and increased viability of APAP-treated primary mouse hepatocytes. Similarly, in mice with APAP-induced ALF, G-CSF dose-dependently improved various outcomes and decreased mortality. We found hepatic G-CSF receptor expression increased after APAP treatment, as shown by immunostaining and western blot studies. In G-CSF-treated mice with APAP-induced ALF, ATM pathway-related gene expression changes improved, and liver necrosis and inflammation, oxidative DNA damage and DNA strand breaks also improved. As p21 expression decreased and Ki67 expression increased at the protein level, this was consistent with reversal of cell growth arrest and onset of hepatic regeneration after G-CSF. Conclusions: Dysregulation of ATM signaling made major contributions to APAP-induced hepatic damage and failure of liver regeneration after ALF. This molecular basis of APAP-induced hepatotoxicity will advance therapeutic strategies.
340 ISOLATED CORTISOL DEFICIENCY: A RARE CAUSE OF NEONATAL CHOLESTASIS.
Abdulrahman A. Al-Hussaini, Awatif Almutairi, Alaaddin Mursi, Ali Asery, Mohammed Alghofely, Pediatrics, King Fahad Medical City, Riyadh, Saudi Arabia

Background and objective: Congenital panhypopituitarism, had caused around 50 cases of cholestasis in neonates and young infants, as reported in the literature. Which hormone deficiency causes such liver derangement is not clear. Some authors suggested that growth hormone deficiency is the major cause of cholestasis. Here, we report our experience with isolated cortisol deficiency manifesting as neonatal cholestasis.

Methods: We reviewed our data base of 350 cases of neonatal cholestasis, presenting to our center during the period from 2007 through 2011. Patients diagnosed with isolated cortisol deficiency were identified and their data were collected by retrospective chart review.

Results: Four males with isolated cortisol deficiency were identified (1%). All presented with biochemical evidence of cholestatic hepatitis (Table 1) and hypoglycemia that led to convulsion in cases 1 and 2. Patients 1 and 2 had generalized hyperpigmented skin. Table 2 shows endocrine investigations during episode of hypoglycemia. On the basis of the hormonal analysis, cases 1 and 2 were diagnosed as familial glucocorticoid deficiency (homozygous mutation in the coding region of ACTH receptor [MC2R] gene), and cases 3 and 4 were diagnosed as isolated ACTH deficiency. Following initiation of hydrocortisone, the hypoglycemia did not recur and skin hyperpigmentation markedly reduced. Cholestasis resolved within 3 months of starting hydrocortisone.

Conclusion: the presentation of a neonate with cholestasis and hypoglycemia should alert pediatricians to the possibility of cortisol deficiency and prompt investigation of adrenal function.

Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at diagnosis (week)</th>
<th>TSB/D (&lt;17/&lt;5 µmol/l)</th>
<th>ALT (30-60 U/l)</th>
<th>GGT (11-60U/l)</th>
<th>Serum bile acid (0-10 umol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>95/76</td>
<td>81</td>
<td>70</td>
<td>9.8</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>141/100</td>
<td>71</td>
<td>35</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>210/160</td>
<td>321</td>
<td>49</td>
<td>144</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>166/137</td>
<td>109</td>
<td>122</td>
<td>171</td>
</tr>
</tbody>
</table>

TSB/D= total bilirubin/direct bilirubin

Table 2

<table>
<thead>
<tr>
<th>Case</th>
<th>Cortisol (83-580 nmol/l)</th>
<th>ACTH (0-13.3 pmol/l)</th>
<th>GH (0-2.6 mlU/L)</th>
<th>Free T4 (12-22 pmol/l)</th>
<th>TSH (1.36-8.8mIU/l)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.21</td>
<td>427</td>
<td>6.77</td>
<td>12.1</td>
<td>6.47</td>
<td>FGD</td>
</tr>
<tr>
<td>2</td>
<td>4.5</td>
<td>391</td>
<td>12.5</td>
<td>16</td>
<td>10.8</td>
<td>FGD</td>
</tr>
<tr>
<td>3</td>
<td>2.7</td>
<td>0.22</td>
<td>9.9</td>
<td>15.3</td>
<td>8.11</td>
<td>ACTH deficiency</td>
</tr>
<tr>
<td>4</td>
<td>3.8</td>
<td>2.5</td>
<td>10.3</td>
<td>19.2</td>
<td>10.3</td>
<td>ACTH deficiency</td>
</tr>
</tbody>
</table>

FGD: familial glucocorticoid deficiency

373* THE EMERGING ROLES OF IL-13 IN CHRONIC COLITIS. Kevin M. O'Meara1,2, Luigi Notari1, Rex Sun1, Jennifer A. Bohl1, Leon McLean1, Shu Yan1, Terez Shea-Donahue1, 1Medicine & MBRC, University of Maryland, Baltimore, MD; 2Pediatrics, Walter Reed National Military Medical Center, Bethesda, MD

IL-13 is increased by nematode infection and exerts protective effects including goblet cell proliferation and the downregulation of Th1/Th17 cytokines. The role of IL-13 in inflammatory pathologies remains unclear, but has been linked to increased mucosal permeability and to fibrosis working in the presence of TNF-α through the decoy receptor, IL-13Rα2. Development of fibrosis involves a balance of degradation of the extracellular matrix (ECM) facilitated by matrix metaloproteinases (MMPs) and decreased turnover of the ECM facilitated by Tissue inhibitors of metaloproteinases (TIMPs). Aim: To define the role of IL-13 in a chronic murine colitis model. Methods: BALB/c mice were given weekly colonic exposure to TNBS (1.5-2.5 mg/mouse) or saline and studied at every other week from 1-13 weeks (W). Previous studies showed that the chronic response develops at about 5W. Sections of colon were prepared for microscopic and real-time PCR analysis. Muscle-free segments of colon were mounted in
microsnapwells to determine transepithelial resistance (TEER), an index of mucosal permeability. Results: IL-13 was upregulated 4-8 fold in the colon from 5 - 13W, coincident with significantly increased mucosal height (p<0.05) and goblet cell proliferation, but no change in TEER. At 13W there was a dramatic change in the appearance of the mucosa with disruption of the epithelium and marked increased cellularity. IL-13Rα2 increased 5 fold at 13W. In addition, there was organized collagen deposition in the submucosal space and upregulation of type 1 collagen, TGFβ1, TGFβ2 as well as increased expression of markers for alternatively activated macrophages (M2). TIMP-1 and TIMP-2 were increased >3 fold at 13W. Conclusions: The results support an acute inflammatory response (<5W) that transitions to an enhanced proliferative response to injury that is mediated by IL-13 until week 13. At this time, the mucosal proliferative response to injury may be supplanted by collagen deposition via a mechanism involving M2 macrophages, TGF-β1 and TIMPs.

374* HIGH THROUGHPUT SCREENING REVEALS A NOVEL EPIGENETIC MICRORNA INFLAMMATORY NETWORK IN PEDIATRIC ULCERATIVE COLITIS. Jess Kaplan1, G. Koukos2, C. Polytarchou2, A. Morley-Fletcher1, C. Pothoulakis3, D. Iliopoulos2, H. S. Winter1, 1MassGeneral Hospital for Children, Boston, MA; 2DFCI, Boston, MA; 3UCLA, Los Angeles, CA

Background: MicroRNAs have been shown to be dysregulated in different human diseases. Their role and function in pediatric IBD has not been elucidated. Here we present a novel microRNA-inflammatory pathway involved in the pathogenesis of pediatric UC. Methods: A microRNA library was transfected in human non-transformed colonic epithelial NCM460 cells to identify regulators of STAT3 activity. RNA was extracted from intestinal tissues of 12 non-inflamed controls and 14 pediatric active UC patients and miR-124 expression was examined by real-time PCR. The interaction between miR-124 and STAT3 was examined by different bioinformatic algorithms. miR-124 promoter methylation status was evaluated by bisulfate sequencing. Results: The microRNA library screen revealed miR-124 as the most potent suppressor (95.5%) of STAT3 activity in NCM460 cells. miR-124 was identified to be highly down-regulated (7.7-fold) in pediatric UC, relative to control tissues. Bioinformatic analysis predicted that miR-124 regulates STAT3 expression through binding in its 3'UTR. MiR-124 over-expression suppressed 45% of STAT3 3'UTR luciferase activity and 82% STAT3 mRNA levels in HCT-116 colonic cells. miR-124 was inversely correlated with STAT3 mRNA levels (correlation coefficient r=−0.912) in pediatric UC tissues. Bisulfite sequencing showed that decreased expression of miR-124 in pediatric UC tissues was due to DNA hypermethylation of its promoter area. Conversely, the miR-124 promoter was completely unmethylated in all control pediatric tissues. 5-Aza-2-deoxycytidine treatment of HCT-116 cells resulted in increased miR-124 expression (5.2-fold) and suppression of STAT3 mRNA levels (4.7-fold). Conclusion: We have identified a novel epigenetic microRNA inflammatory pathway in pediatric UC, whereby DNA methylation suppresses miR-124 expression, resulting in activation of an inflammatory response through STAT3 phosphorylation. Supported by a grant from the Pediatric IBD Foundation

375 OVERWEIGHT AND OBESITY IN CHILDREN WITH SEVERE INFLAMMATORY BOWEL DISEASE (IBD) TREATED WITH INFliximAB: A RETROSPECTIVE COHORT STUDY. Vera Okwu, Jonathan Moses, Sarah Worley, Naim Alkhouri, Pediatric Gastroenterology, Cleveland Clinic Children's Hospital, Cleveland, OH

BACKGROUND: Inflammatory bowel disease (IBD) patients have traditionally been viewed as underweight/malnourished but the phenotype is changing rapidly and new studies show higher prevalence of overweight/obesity in these patients. Infliximab is used to treat severe IBD and recent evidence suggests that it may lead to excessive weight gain in a subset of IBD patients.

AIMS: 1) To assess the baseline prevalence of overweight/obese in children with severe IBD treated with infliximab; 2) to assess the trend in body mass index (BMI) over the course of treatment with infliximab, and 3) to evaluate for potential predictors of overweight/obese status in this cohort at the last follow-up visit.

METHODS: Baseline demographics, clinical characteristics, annual height, weight, BMI and BMI percentile measurements were obtained for 97 IBD patients [89 Crohn's disease (CD) and 8 ulcerative colitis (UC)] treated with Infliximab. Overweight was defined as BMI ≥ 85% for age and obese was defined as BMI ≥ 95% for age. RESULTS: Median age at treatment was 15 years (range: 6-23) with a median length of follow-up of 4 years (range: 3mo-8yrs). At start of treatment 10% were underweight, 75% had normal BMI and 15% were overweight/obese. At the last follow-up visit 24% were overweight/obese. Median change in BMI from baseline was 0.54 (-10.6, 26.2) percentile points for the entire cohort and 11.3 (0.58, 32.2) for the overweight/obese group. Of the patients that became overweight/obese 30% had IBD surgery vs 13% of the other patients and 60% had a history of steroid use vs 84% of the other patients. Patient characteristics significantly associated with being overweight/obese at final follow-up visit were abnormal liver function tests, higher hemoglobin and baseline BMI.

CONCLUSION: A significant percentage of children with severe IBD are overweight/obese at baseline and may become overweight/obese while being treated with Infliximab. These patients should be screened for obesity-related morbidities including fatty liver disease.
376 CEREBRAL THROMBOEMBOLISM IN PEDIATRIC ULCERATIVE COLITIS: A CASE SERIES.  
Melissa Rose, Vesta Salehi, Thomas Ciecierega, Aliza Solomon, Robbyn Sockolow, Cornell Medical College, New York, NY  
Background: Prior studies have shown an increased risk of thromboembolism (TE) in patients with inflammatory bowel disease, and especially in ulcerative colitis (UC) (1). Though both are rare complications, peripheral TE is more common than cerebral TE. Risk factors for TE are likely multifactorial and may include disease activity and coagulation abnormalities (2, 3).  
Case Series: We report on a 6 year old female and 12 year old male with UC who developed cerebral vein TE. PUCAI at the time of TE was 60 and 25, respectively. Both patients presented with acute, non-focal neurologic exams and complaints including headache and unilateral eye pain. Evaluation was significant for protein S deficiency in both. Additionally, one patient was heterozygous for the prothrombin G20210A mutation and homozygous for the PAI-1 mutation. Both were admitted to our Pediatric Intensive Care Unit where they received anticoagulation with Enoxaparin 1mg/kg/dose given twice daily that was titrated to a therapeutic level of 0.8-1.0. Disease control was improved with the initiation of infliximab in one patient (PUCAI 60 to 25) and prednisone with 6-MP in the other (PUCAI 25 to 0). Both patients had an excellent response and full neurologic recovery without bleeding on anticoagulation therapy.  
Conclusion: Cerebral thromboembolic complications are fortunately rare occurrences in pediatric UC patients, however it is suggested that both disease activity and hypercoagulable state are risk factors. Anticoagulation and appropriate pharmacologic therapy are key in effective treatment of TE in these patients.  

377 PRE-OPERATIVE NUTRITIONAL STATUS AND IMMUNOSUPPRESSION AS PREDICTORS OF POST-OPERATIVE EVENTS IN PEDIATRIC CROHN'S DISEASE PATIENTS. Melissa Rose, Vesta Salehi, Aliza Solomon, Robbyn Sockolow, Cornell Medical College, New York, NY  
Objective: To evaluate the frequency of post-operative complications in children with Crohn's disease (CD) in relation to nutritional status and use of immunosuppressive medications prior to surgery.  
Patients/Methods: A case series was conducted of 13 pediatric patients with CD who underwent surgical intervention from 2007-2011. Time from diagnosis to first surgical intervention, type of surgery, pre-operative immunosuppression and nutritional status, and post-operative complications were reviewed.  
Results: Average time from diagnosis to first surgical intervention was 2.63 years. Procedures included four partial colectomies, two partial colectomies with stricturoplasty and one with partial jejunal resection, one total colectomy with ileostomy, one ileostomy without colectomy, and five procedures for perianal disease. Five patients had additional surgical procedures including total colectomy with ileostomy, partial colectomy, and fistulotomy. Eight patients had elective and five had emergent procedures. Reasons for emergent surgery included severe anemia and pain; small bowel obstruction (two patients); persistent pain; and bowel perforation. Five patients were on immunosuppressive medications at the time of surgery; two were on immunomodulators (IM), one on biologics, one on steroids/biologics, and one on steroids/IM. Six patients had been off of immunosuppression for 2-8 weeks and two had never been on immunosuppression. Four patients had a BMI <5th percentile at the time of surgery.  
Short-term (<30 days) post-operative events occurred in two patients with recurrent perianal disease requiring repeat surgery (normal BMI, on IM or biologics). Long-term (30-180 days) post-operative events included repeat surgery (normal BMI, on steroids/biologics), and rectal bleeding requiring readmission (normal BMI, on biologics). One patient had an anastomotic stricture, however this was at >2 years.  
Conclusions: Immunosuppression is more common than malnutrition in pediatric patients with Crohn's disease who have post-operative events.

378 ALEXITHYMIA IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE.  
Jaime D. Crowley1, Crista E. Wetherington2,1, Gabriela M. Reed2,1, Sunita Stewart2,1, Ashish Patel1, Stephen Robertson1, Lauren C. Smith1, 1UT Southwestern Medical Center, Dallas, TX, 2Psychiatry, Children's Medical Center, Dallas, TX  
Adolescents with Inflammatory Bowel Disease (IBD) exhibit increased psychological problems, such as higher rates of depressive symptoms. Alexithymia, defined as a personality trait and affective deficit disorder, may represent another variable influencing emotional wellbeing in IBD. While no prior studies have investigated alexithymia in adolescents with IBD, research shows significant rates of alexithymia among adults with IBD. Higher rates of alexithymia have been associated with poorer quality of life (QOL) in adult IBD patients. This study investigated the...
prevalence of alexithymia in adolescents with IBD and examined the relationship between alexithymia and other psychological variables (i.e., depressive symptoms and perceived stress). An investigation of 63 participants with IBD between the ages of 13 to 17 years revealed a significant prevalence of alexithymia compared to rates found in a previously documented normal adolescent population. However, the rate of alexithymia in this adolescent study sample was significantly lower than rates previously reported in the adult IBD population. Higher alexithymia scores were associated with higher scores on depressive symptoms, perceived stress of major life events, perceived stress of daily hassles, and perceived recent stress. The potential lifelong repercussions of alexithymia make it an important topic for adolescent IBD research. Given the relationship between alexithymia and other psychological variables, future alexithymia research may guide the development of psychological interventions in this pediatric illness population.

379 ASSOCIATION OF GROWTH AND NUTRITIONAL STATUS WITH PEDIATRIC ULCERATIVE COLITIS ACTIVITY INDEX, INDICATORS OF SYSTEMIC INFLAMMATION AND STEROID TREATMENT IN CHILDREN WITH ULCERATIVE COLITIS. Fabiola Barba- Munguía1, Rocío Macías-Rosales1, Alfredo Larrosa-Haro2, 1Gastroenterology and Nutrition, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Centro Universitario en Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

Aim: To evaluate the association of growth and nutritional status with the Pediatric Ulcerative Colitis Activity Index (PUCAI), indicators of systemic inflammation and steroid treatment in children and adolescents with ulcerative colitis (UC).


Results: PUCAI score was >10 in 54%. Platelet count was above normal 7 patients, 9 patients (63%) had elevated ESR and 3 (23%) had increased C-reactive protein. The median cumulative dose of corticosteroids was 14,070 mg and the median administration time was 25 months; the total dose of corticosteroids was 3-4 times higher than recommended. Corticosteroid time administration correlated significantly with BMI z-score. No correlation was found between inflammation markers and nutritional status.

Conclusions: The high frequency of cases with PUCAI >10 and of altered inflammatory markers indicate poor disease control, probably related to a poor response to azathioprine and underlying low thiopurine methyltransferase activity. Prednisone dependence could also be related to this hypothetical condition. No significant impairment of the nutritional status and growth was demonstrated with the exception of BMI with the cumulative dose of corticosteroids, suggesting increased fat deposits induced by this drug.

Concurrent Session IV – IBD II

Saturday, October 20, 2012

388 INTESTINAL MICROBIOME DIVERSITY AND OUTCOMES IN PRETERM HUMAN INFANTS

Mem Zolak1, Ian Carroll2, Philip Tatum1, Thomas Soltau1, Reed A. Dimmitt1, 1Pediatrics, University of Alabama at Birmingham, Birmingham, AL; 2Medicine, University of North Carolina, Chapel Hill, NC

Background: Differences in the perinatal period may alter the preterm intestinal microbiome. Studies have suggested probiotic bacteria may prevent diseases of prematurity, specifically necrotizing enterocolitis (NEC). The purpose of this study was to define the preterm intestinal microbiome in relationship to perinatal factors and outcomes.

Methods and Materials: Weekly fecal samples were obtained for 8 weeks or until discharge from 126 preterm patients. DNA was extracted from the samples and amplified using a barcoded primer set containing the 454 Life Sciences® 16s ribosomal primers. The purified product was sequenced using Roche 454 Genome Sequencer®. Sequences were analyzed with quantitative the insights into microbial ecology (QIIME) pipeline. Patient data included gestational age, birth weight, gender, maternal race, presence of maternal prolonged rupture of membranes, mode of delivery, feeding substrate including timing of first feeding, all antibiotic courses, development of NEC, bacteremia, bronchopulmonary dysplasia (BPD), and survival. Univariate and multivariate analyses were performed, p<0.5 significant.

Results: Overall, there was marked lack of microbiome diversity in the samples. Patients with less diversity had worse outcomes. Patients with <50% Enterobacteriaceae sp. had significantly greater survival and less NEC than infants with ≥ 50% Enterobacteriaceae sp. In addition, the bacterial diversity decreased significantly prior to development of NEC and abundance of Proteobacteria increased over time in infants that developed NEC. The percentage of intestinal Mycoplasma was low but significantly higher in patients that developed BPD. No demographic or clinical data predicted microbiome composition or outcome.

Conclusion: Intestinal microbiome diversity is associated with reduced morbidity and mortality in preterm infants. Further studies regarding probiotic and prebiotic therapy may provide mechanisms to promote a normal intestinal
lymphocyte function in colitis, we activated mesenteric lymph node (MLN) cells in the presence or absence of MLN cells from colitic WT mice compared to healthy WT mice, suggesting colitis may prime lymphocytes to respond to IL-33. These data implicate STAT6 in the pathogenesis of colitis in vivo with important roles in altering epithelial barrier function and regulating Th2-inducing cytokine production.

Expression of IL-13, IFN-γ, IL-17, and IL-10 mRNA was similarly induced in WT and STAT6-/- colitic mice; however, we observed increased expression of the Th2-inducing cytokines IL-33 and thymic stromal lymphopoietin (TSLP) in WT mice with colitis, which was abrogated in STAT6-/- mice. To determine the effect of IL-33 on lymphocyte function in colitis, we activated mesenteric lymph node (MLN) cells in the presence or absence of recombinant IL-33. IL-33 induced IL-4, IL-5, IL-13, IL-6, IFN-γ and IL-10 secretion to a much greater degree in MLN cells from colitic WT mice compared to healthy WT mice, suggesting colitis may prime lymphocytes to respond to IL-33. These data implicate STAT6 in the pathogenesis of colitis in vivo with important roles in altering epithelial barrier function and regulating Th2-inducing cytokine production.

Glutamine (GLN) is a key fuel for the continuous and dynamic renewal of the intestinal epithelium. However, distinct effects of GLN on the intestinal epithelial stem cells (ISC) that reside in the crypts of Lieberkuhn have not yet been described. We found that oral administration of alanyl-glutamine (ALA-GLN) to undernourished mice protects the jejunal epithelium against malnutrition-associated reductions in crypt counts. We further found that jejunal organoids derived from malnourished mice and controls are equally viable; however, GLN or ALA-GLN—but not other non-essential amino acids—are required for organoids to proliferate, expand, and maintain a stable crypt-villous architecture. When deprived of GLN, organoids from mice with EGFP labeling of ISC marker Lgr5 demonstrate minimal changes in Lgr5 expression, but exhibit a decrease in epithelial proliferation, followed by an increase in apoptosis, atrophy of crypt domains, and eventual collapse. Despite these dramatic effects, viable Lgr5+ stem cells persist up to 7 days following GLN deprivation. Upon reintroduction of GLN, Lgr5+ stem cells reactivate to replenish the organoid epithelium. These findings indicate that GLN deprivation induces a reversible quiescence of Lgr5+ intestinal stem cells and have important implications for nutritional regulation of intestinal epithelial homeostasis.

Colonic DNA methylation and microbiota associations of aging and ulcerative colitis in untreated children. Richard Kellermayer1, Dorotya Nagy-Szakal1, R. A. Harris2, Scot E. Dowd2, Sabina A. Mir3, Jess L. Kaplan4, Harland S. Winter5, 1Section of Pediatric Gastroenterology, Baylor College of Medicine, Houston, TX; 2Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; 3Molecular Research, Shallowater, TX; 4Department of Pediatrics, MassGeneral Hospital for Children, Boston, MA

BACKGROUND & AIMS: Inflammatory bowel diseases (IBD) are emerging globally supporting the hypothesis that environmental factors may play a role in their pathogenesis. Commensal microbes and epigenetic characteristics, such as DNA methylation can respond to environmental changes and have been implicated in triggering these diseases during critical developmental periods. Therefore, we evaluated the relationship between colonic mucosal microbiota and DNA methylation in pediatric IBD. METHODS: The mucosal microbiota was studied by 454 pyrosequencing of the bacterial 16S rRNA gene and the fungal small subunit (SSU) ribosomal region in transverse colonic biopsy specimens from 26 controls, 16 pediatric CD (15 treatment naive), and 6 UC cases (5 treatment naive). Genome-wide DNA methylation was examined by Infinium HumanMethylation450 BeadChip Kits in a subset (10 controls, 10 CD, and 4 UC). Validation of the DNA methylation results by bisulfite-pyrosequencing was expanded to 8 UC patients at select loci. RESULTS: There was more significant DNA methylation in preterm infants.
methylation association of UC (8244 CpG sites) than CD (3 CpG sites) (FDR<0.01). The UC-linked methylation changes associated with genes involved in immune responses, and overlapped with 58.4% of earlier reported UC specific gene expression in discordant monozygotic twins. UC specific and age dependent DNA methylation changes overlapped at 22 genes. UC microbiota separated from controls and CD (p=0.048). The genus *Faecalibacterium* was specifically increased in UC. Age and UC dependent microbiota changes overlapped in respect to *Bacteroides capillosus* and *Fusobacterium periodonticum*. CONCLUSIONS: Age and UC associated DNA methylation and microbiota changes overlap at select loci and taxa. These findings may have etiologic, diagnostic and therapeutic relevance for IBD.

**Concurrent Session IV – Motility/Functional Gastrointestinal Disorders**

**392 TRPV1 MEDIATES ANXIOUS/DEPRESSIVE BEHAVIOR IN A MURINE MODEL OF POST-INFECTION ABDOMINAL PAIN.** John Rosen1, David J. Klumpp2, 1Pediatric GI and Hepatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2Urology and Microbiology-Immunology, Northwestern University Feinberg School of Medicine, Chicago, IL.

Background: Gastrointestinal and genitourinary pain syndromes, including irritable bowel syndrome (IBS) and interstitial cystitis, have significant clinical overlap and are associated with increased anxiety and depression. The transient receptor potential vanilloid type 1 (TRPV1) channel is distributed widely and is upregulated and/or sensitized in several non-inflammatory chronic pain states including IBS. In vitro evidence suggests Gram-negative bacteria play a role in TRPV1-induced pain through TLR4-dependent mechanisms. Our laboratory recently demonstrated that TLR4-dependent, inflammation-independent chronic pain can be induced by SΦ874, a K12 bacteria lacking O-antigen.

Hypothesis: TRPV1 mediates urinary tract infection (UTI) associated chronic abdominal pain.

Methods: We administered subcutaneous capsazepine (TRPV1 antagonist) or vehicle to mice also administered transurethral SΦ874 (UTI) or saline control. Allodynia was quantified 14 days after infection by von Frey filament testing in the lower abdomen. Anxiety and depression were assessed with the novelty suppressed feeding behavioral test.

Results: Allodynia induced by SΦ874 was not significantly reduced by capsazepine. Anxiety/depression increased for mice with SΦ874 infection, but did not develop in mice receiving capsazepine (p<0.05, ANOVA).

Conclusion: We demonstrated increased anxious/depressive behavior in mice with post-infection chronic abdominal pain. However, capsazepine anxiety/depression reduction was not correlated with a decrease in pain. TRPV1 in the central nervous system, known to regulate emotion, may affect anxious/depressive behavior in the setting of chronic abdominal pain.

**393 THE UTILITY OF ACOUSTIC COUGH RECORDING AND INTRAESOPHAGEAL PRESSURE MONITORING FOR THE DETECTION OF COUGH DURING PH-MII TESTING.** Rachel L. Rosen1, Nicole Heinz2, Janine Amirault1, Jerry Mabary2, Samuel Nurko1, 1Children's Hospital Boston, Boston, MA; 2Sandhill Scientific, Highlands Ranch, CO.

Background: The ability to correlate symptoms with reflux during pH-MII testing is limited by the ability of patients to accurately record symptoms. This study will validate the use of acoustic recording (AR) and compare it to intraesophageal pressure (EP) monitoring and patient report (PR) for the detection of cough.

Methods: We performed AR in treated children undergoing combined pH-MII testing and 4 channel EP monitoring for the evaluation of cough. Blinded reviewers coded each AR and EP cough independently. The AR, EP and pH-MII studies were then merged to determine the sensitivity of the technologies to detect cough. Symptom correlation with reflux was performed using a 2 minute window.

Results: 632 total coughs were analyzed; 605 were detected by AR, 549 were detected by EP, and 173 were PR coughs. The detection overlap is shown in the Table. Using AR as the gold standard, the sensitivity of PR for the detection of cough was 26%. The sensitivity of EP for the detection of cough was 89%. The mean time from an AR to a PR cough was 5.4±7.2 seconds. 119/632 (19%) coughs were associated with reflux; 41% of the time, reflux preceded cough and, 59% of the time, cough preceded reflux. 92% of cough-associated reflux episodes were non-acidic, 0.8% were acidic and 7.2% were pH only events. 9% of reflux episodes associated with cough were full column. The mean time from an AR cough to a reflux event was 57±36 seconds.

Conclusions: AR detects 3.5 times the number of coughs than PR alone and correlates well with EP monitoring. AR is a sensitive, non-invasive tool that may improve reflux-cough correlations.
The number (%) of coughs detected by AR, EP and PR.

<table>
<thead>
<tr>
<th>Combination</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR+EP+PR</td>
<td>145</td>
<td>23%</td>
</tr>
<tr>
<td>AR+EP</td>
<td>394</td>
<td>62.3%</td>
</tr>
<tr>
<td>AR+PR</td>
<td>11</td>
<td>1.7%</td>
</tr>
<tr>
<td>EP+PR</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>AR</td>
<td>55</td>
<td>8.7%</td>
</tr>
<tr>
<td>CC</td>
<td>10</td>
<td>1.6%</td>
</tr>
<tr>
<td>PR</td>
<td>17</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

Neurogastroenterology and Motility Prize

394  NESTIN EXPRESSING CELLS FROM ALL INTESTINAL LAYERS GIVE RISE TO PLURIPOTENT NEUROSPHERES THAT GIVE RISE TO NEURONS UPON TRANSPLANTATION.
Jaime Belkind-Gerson¹, Alfonso Carreon-Rodriguez², Leo Andrew Benedict², Casey E. Steiger², Alberto C. Pieretti², Nandor Nagy², Alan M. Goldstein², ¹Pediatric GI, MGH, Boston, MA; ²Pediatric Surgery, Massachusetts General Hospital, Boston, MA

Introduction: Nestin expressing Neural stem cells (NSCs) in brain are important in regeneration. Nestin cells are present in all gut layers. We and others have cultured NSCs from gut, but the role of Nestin in the enteric NSCs is unknown.

Aims: To determine if Nestin-expressing cells in the different intestinal layers are capable of giving rise to pluripotent NSCs that then give rise to new neurons upon transplantation.

Methods: Single cells from peri-ventricular brain, colonic muscularis and mucosa-submucosal layer of adult mice expressing Nestin-GFP were grown in serum-free media with EGF and bFGF to give rise to Neurospheres grown in proliferation media for 7 days. Expression of pluripotency markers Sox2, cMyc and Klf4 was measured by quantitative PCR. Cells were then differentiated. Neuronal and glial differentiation was investigated immunohistochemically. NSCs were transplanted into aneural chicken embryonic hindgut to determine cell fate ex vivo.

Results: 1) Nestin expression was abundant in mucosa, submucosal plexus and myenteric ganglia. 2) The majority of Nestin+ cells in the gut expressed glial markers GFAP or S-100. 3) All gut and brain-derived neurospheres were GFP+. 4) The proliferating neurospheres from mucosa-submucosa, muscularis and brain express Sox2, cMyc and Klf4. 4) When brain and enteric NSCs differentiated, they gave rise to glial and neuronal networks. 5) Both types of NSCs gave rise to neurons ex vivo when transplanted into aneural chicken hindgut.

Conclusions: Brain- and gut-derived NSCs share similarities: Both arise from Nestin+ cells and as neurospheres, they maintain Nestin expression. They also express the pluripotency markers Sox2, cMyc and Klf4. Both types of neurospheres can be successfully transplanted into the aneural chick hindgut, where they give rise to new neurons.

The coexpression of nestin and glial markers in the intestine suggests that, as in brain the NSCs may be glial-derived.

395  ROLE OF PERIAQUEDUCTAL GRAY NMDA AND µ-OPIOID RECEPTORS IN SLEEP INTERRUPTION INDUCED VISCERAL HYPERALGIESIA. Mitch Bruckert, Pradeep Kannampalli, Sounya Pochiraju, Banani Banerjee, Jyoti N. Sengupta, Adrian Miranda, Medical College of Wisconsin, Milwaukee, WI

Introduction: Recent reports indicate a direct and opposing association between the µ-opioid receptor (MOR) and the N-methyl-D-aspartate (NMDA) receptor in regulating the descending opioidergic pain pathway. Our clinical data suggests that melatonin (MEL) improves abdominal pain independent of changes in sleep. We set out to investigate the role of these receptors in the development of visceral hyperalgiesia following sleep interruption (SI) and to determine the mechanism involved in MEL anti-nociception. Methods: Male Long-Evans rats were subjected to SI during the 12 hour "lights-on" period (cage oscillation every 90sec) for 2 days. A visceromotor response (VMR’s) to colorectal distension (CRD, 10-60mmHg) was recorded before and after SI. MEL (10nmol) was injected into the periaqueductal gray (PAG) post SI (n=5). In a different group (n=5), naloxone, a selective MOR antagonist, was injected (10µg/side, intra-PAG) 30 minutes prior to MEL injection (60mg/kg i.p.). In a separate group (n=5), antisense oligonucleotide (ODN) was used to knock down the NR1 subunit in the PAG. Injections were given intra-PAG twice daily (10µmol/side) for five days. VMR was recorded following SI on the final 2 days. NR1 expression in the PAG was examined using Western blot in naïve and SI rats (n=8). Results: SI significantly increased the VMR at CRD pressures >30mmHg (p<0.05) and was decreased by MEL (p<0.05). Intra-PAG naloxone effectively blocked the analgesic properties of MEL at all CRD pressures, however, MEL given intra-PAG was ineffective in producing analgesia post SI. The anti-NR1 ODN prevented the development of visceral hyperalgiesia following SI.
Compared to control, NR1 expression in PAG of SI rats was significantly higher (p<0.05). Conclusion: SI induced visceral hyperalgesia is regulated through NMDA receptors in the PAG and not directly by melatonin receptors. The anti-nociceptive effect of MEL likely involves the MOR pathway in the PAG and further suggests an interaction between the NMDA and MOR in the descending modulatory pain pathway.

Concurrent Session V – Liver Disease
Saturday, October 20, 2012

396 HIGH DOSE IGG THERAPY RESULTS IN DIMINISHEDBILE DUCT INFLAMMATION IN EXPERIMENTAL BILIARY ATRESIA. Juri Boguniewicz1, E. K. Peiffer1, R. M. Tucker1, R. J. Sokol1,2, C. L. Mack1,2, 1University of Colorado School of Medicine, Aurora, CO; 2Children’s Hospital Colorado, Aurora, CO
Background: A proposed etiology of biliary atresia (BA) suggests that a viral insult initiates bile duct injury, followed by progressive immune-mediated inflammation and fibrosis. High dose intravenous polyclonal immunoglobulin (IVIg) has demonstrated clinical benefit in several inflammatory diseases. Aim: To determine if bile duct inflammation and injury is diminished with high dose immunoglobulin (IgG) treatment in a mouse model of BA. Methods: Neonatal BALB/c mice were injected with rhesus rotavirus (RRV) or control Hanke's Balanced Salt Solution (BSS) 12-18 hours after birth. On day 7, 9, 11 RRV-infected, jaundiced mice were given intraperitoneal injections of high dose IgG (2 g/kg) or albumin (alb.) control. Survival, liver and bile duct histology, direct bilirubin levels, liver immune cell subsets and cytokine production were analyzed in all groups (BSS, RRV, RRV-alb, RRV-IgG). Results: High dose IgG did not significantly improve overall survival in BA mice at 2 weeks of age. However, histology showed markedly reduced portal tract and extrahepatic bile duct inflammation in the RRV-IgG mice and significant decreases in direct bilirubin levels were observed in the RRV-IgG group (BSS: 0.19±0.09; RRV: 11.02±0.9; RRV-alb: 9.78±1.0; RRV-IgG: 4.75±0.7 mg/dL) (p<0.001). Intracellular cytokine staining revealed significantly lower levels of IL-2, IFN-γ and TNF-α production by liver CD4+ T cells in RRV-IgG mice compared to infected controls (RRV and RRV-alb groups). A significant increase in liver regulatory T cells (Tregs) was also observed in the RRV-IgG group compared to infected controls (BSS: 9.4±0.5; RRV: 5.8±0.5; RRV-alb: 7.5±0.03; RRV-IgG: 10.3±0.7% Tregs) (p<0.01). Conclusions: Immune therapy with high dose IgG was associated with decreased inflammation and injury of the bile ducts in the mouse model of BA. The expansion of Tregs and associated decrease in CD4+ T cell cytokine production identified in high dose IgG-treated BA mice points to a possible mechanism of action for IVIg therapy in human BA.

397 GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONIST EXENDIN 4 (EX4) PROTECTS STEATOTIC HEPATOCYTES FROM ISCHEMIA REPERFUSION INJURY BY MITIGATING AUTOPHAGY. Nitika A. Gupta1,2, Vasantha L. Kolachala1, Rong Jiang1, Carlos Abramowsky1,2, Allan Kirk1,2
1Division of Pediatric Gastroenterology, Emory University School of Medicine, Atlanta, GA; 2Transplant Services, Childrens Healthcare of Atlanta, Atlanta, GA; 3Department of Pathology, Emory University School of Medicine, Atlanta, GA
Background: With increasing obesity, a large proportion of livers undergoing ischemia reperfusion injury (IRI), are steatotic and exquisitely susceptible to cell death. Autophagy is a tightly regulated lysosomal pathway with incompletely elucidated functions of survival and death. Methods to modulate autophagy would improve outcomes of IRI of a fatty liver and increase donor pool. Aim: To evaluate autophagic responses in IRI of a steatotic liver and the role of Ex4 in modulating these pathways. Methods: C57BL/6 mice were fed a high fat diet (HFD) and subjected to IRI along with Ex4 treatment. HuH 7 cells were made steatotic, exposed to hypoxia/ischemia/reperfusion and treated with Ex4. Exendin 9-39, a GLP-1R antagonist was used to block GLP-1 signaling. LC3 II and beclin 1 expression was assessed, serum ALT was measured and liver mitochondria were examined under electron microscopy. Results: At baseline, there was a low expression of LC3 II in HFD mice as compared to lean mice. After IRI, LCII expression significantly increased in the HFD group (7.5±3.1vs1.0±0.3 RDU;p<0.01). Serum ALT levels were higher post IRI in HFD mice (700±43vs183±12 IU/l;p<0.01).Treatment with Ex4 lead to a significant reduction of LCII in HFD mice undergoing IRI (1.2±0.3vs7.5±3.1 RDU;p<0.01) with concomitant lower serum ALT levels (116±31 IU/l;p<0.004). Similarly, in steatotic hepatocytes undergoing hypoxic/ischemic/reperfusion injury, Ex4 treatment decreased LCII expression as compared to non-treated cells (0.2±0.04 vs0.4±0.05 RDU; p<0.02). Use of Ex9-39 reversed this effect (0.37±0.06; p<0.01). Beclin1 showed a similar trend with levels decreasing with Ex4 treatment (0.25±0.05vs0.52±0.02; p<0.01), the effect being reversed by Ex9-39 (0.45±0.08; p<0.02). Mitochondrial cristae were destroyed after IRI of HFD mice and completely preserved with Ex4 treatment. Conclusion: Exendin 4 mitigates autophagy which is increased in steatotic livers undergoing IRI and decreases hepatocellular damage. Thus, in the setting of steatotic IRI, autophagy is detrimental and developing therapeutic targets to decrease it will lead to improved outcomes.
398 LIPID PROFILES AND LIVER STEATOSIS IN CHILDREN WITH LIVER TRANSPLANTATION FOR BYLER'S DISEASE. Ana Catalina Arce Clachar1, Jonathan Moses1, Gursimran Kochhar2, Peggy George2, Srinivasan Dasarathy2, Vera Hupertz1, Kadakkal Radhakrishnan1, Naim Alkhouri1,2

1Pediatric Gastroenterology Department, Cleveland Clinic Children's Hospital, Cleveland, OH; 2Digestive Disease Institute, Cleveland Clinic, Cleveland, OH

Background: Byler's disease is an autosomal recessive syndrome in which patients develop progressive cholestatic liver disease often requiring liver transplantation during childhood. Severe liver steatosis is a common complication post transplantation with no clear etiology. We aimed to evaluate lipid profiles in children who received liver transplantation for Byler's disease and their correlation with hepatic steatosis.

Methods: A retrospective review of children who received a liver transplantation at the Cleveland Clinic was done. Patients who were transplanted for Byler's disease were identified and were matched in a 1:2 ratio with patients transplanted for other indications. Lipid profiles were compared in the 2 groups. P value < 0.05 was considered statistically significant.

Results: Five children with Byler's disease and 10 children with other indications for liver transplantation were included in the study. Liver biopsies of the transplanted livers demonstrated that all children with Byler's disease had moderate-to-severe steatosis, 3/5 had steatohepatitis, and 2/5 had bridging fibrosis. Interestingly, the Byler's disease group had significantly lower HDL levels post transplantation compared to the other group (20.9 ± 6.0 mg/dL vs. 51.3 ± 17.1 mg/dL, respectively, p < 0.001). There was no significant difference in LDL, VLDL or TG. Total cholesterol was also lower in the Byler's group (72 ± 8.0 vs. 156 ± 103, p < 0.001) but this could be a reflection of the lower HDL levels.

Conclusion: Liver steatosis and low HDL levels are consistent findings in children post liver transplantation for Byler's disease. The mechanistic pathways leading to these complications should be investigated in future studies.

399 IMPACTS OF A SHORT-TERM, METROPOLITAN, LOW-COST, SUMMER DAY-WELLNESS CAMP IN PEDIATRIC OBESITY MANAGEMENT. Amanda Garant2, Zhuokai Li2, Joan Servaas1, Jamie Brubaker1, Pat Perry1, Ann Laggess1, Kyle McIlrath1, Amanda McDowell1, Sandeep Gupta2, 1The Children's Better Health Institute, Indianapolis, IN; 2Riley Hospital for Children, Indianapolis, IN

Rates of pediatric obesity/overweight in the US have tripled to a current prevalence of 30%. Obese youth have an 80% probability of being an obese adult and weight management interventions should be multi-disciplinary with frequent contacts between patients/providers. This study reports results of a low-cost, metropolitan, six-week summer day-wellness camp, Forever Fit (FF).

Methods: Children ages 8-12 years, with BMI >95th%ile for age/gender were enrolled in FF and educated on healthy nutrition/physical activity. Pre-and-post camp assessments were completed at the first and last week of the camp and included: ht, wt, BMI (kg/m2), waist/arm circumference and fitness assessments. Parental involvement was highly encouraged. Pre- and post- assessments were compared by using paired t-tests and random intercept Poisson mixed model.

Results: 26 participants were enrolled; 15 had pre-and post-intervention data for analysis; mean age 10.27 yrs; 5 (33%) males; 10(67%) AA and 5(33%) Caucasian; mean initial BMI was 33.27 and mean post- BMI 30.81. 78.9% of children were of urban demography. After intervention, BMI decreased by a mean of 2.45 (p=0.002) and core strength increased by 1.40 sit ups (p=0.003). While resting heart rate decreased by 18.5 per child (p=0.003), the three minute step test heart rate did not significantly change. BMI loss was seen regardless of race. Using the 10yrs group (1.49 loss) as reference, the older (11-12yrs) and younger (8-9yrs) showed a greater BMI loss of 3.53 (p=0.011) and 2.97 (p=0.036).

Conclusions: FF camp improved BMI/ physical assessments of children with obesity. The results underscore the need to engage children and families in managing weight and lifestyle habits in a multi-disciplinary setting, and encourage providers to evaluate non-hospital based, off-site, low-cost alternatives to childhood obesity management. Long-term follow-up to evaluate persistence of BMI changes and trends in healthy habits is on-going.